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# ROENTGEN THERAPY AS THE SOLE METHOD OF TREATMENT OF CANCER OF THE BREAST*

*By* DR. F. BACLESSE
*Fondation Curie*
PARIS, FRANCE

THE use of roentgen therapy as the sole method of treatment in cancer of the breast is based on the results obtained from the use of preoperative roentgen therapy in high dosage, followed by radical mastectomy.

The following is a table correlating the histopathological effect of irradiation on the tumor with the five year results in 58 cases treated with roentgen therapy plus radical surgery from 1936 to 1942 at the Curie Foundation (Table 1).

Table 1 shows three important facts. (1) The cases in which the tumor was histopathologically completely sterilized or in which it was *almost* completely sterilized have given no local recurrence. (2) Recurrences appeared only in the advanced

TABLE I

MAMMARY CANCER; ROENTGEN THERAPY PLUS SURGERY (HALSTED); FIVE YEAR RESULTS

| Histopathology | No. of Treated Cases | Clinical Healing after 5 Years | Local Recurrence | Died of Metastasis | Died of Intercurrent Disease | Untraced | Postoperative Death |
|---|---|---|---|---|---|---|---|
| Complete cell death | 12 | 8 | | 3 | 1 | | |
| Questionable cell death | 8 | 4 | | 3 | | 1 | |
| Marked histopathological change | 13 | 6 | | 6 | | | 1 |
| Moderate histopathological change | 25 | 9 | 7 | 8 | 2 | | 5 |
| Total | 58 | 27 | 7 | 20 | 3 | 1 | 6 |

Five year results of 58 cases (Stages II and III), treated by roentgen therapy with high doses, followed by radical mastectomy (1936–1942).

* Presented in a Panel Discussion on Treatment and Results in Cancer of the Breast at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

cases where the histopathological changes as a result of therapy were not so marked, and of special interest is the fact that all

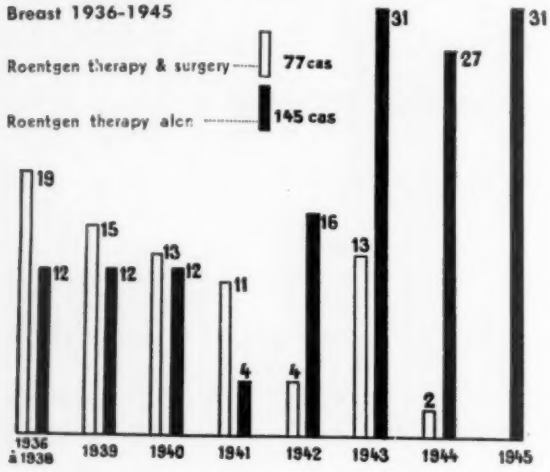


FIG. 1. Number of cases of cancer of the breast treated by each method in the years 1936–1945.

the local recurrences were associated with distant metastases. (3) Moreover, these advanced cases, irradiated with high doses and then operated upon, have produced 5 postoperative deaths. Thus, it is apparent that an advanced cancer, highly irradiated, must not be operated upon except in very special instances, because there is danger of local recurrence associated with distant metastases, and there is a high percentage of postoperative deaths.

In the case of the axillary lymph nodes the results are not so evident, as lower doses must be given in view of the contemplated extensive dissection, and these lower doses will not produce sterilization except in rare cases of very sensitive tumors (Table II).

Figure 1 shows the evolution of the radiotherapeutic method in one roentgen-ray department of the Curie Foundation, from 1936 to 1945. It is noted in this figure that a progressively greater percentage of cases is being treated by roentgen therapy alone.

In the first part of this paper we will discuss the immediate results after one, three, and five years, in mammary tumors, the axillary lymph nodes, and the supraclavicular lymph nodes, all considered separately. This is the analysis of the local and regional problem. These results will show

TABLE II

MAMMARY CANCER; ROENTGEN THERAPY PLUS SURGERY (HALSTED); FIVE YEAR RESULTS

| | Stage II | | | | | | | Stage III | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Histopathology | Number of cases treated | Clinical healing after 5 years | Died of local recurrence | Died of metastases | Died of intercurrent disease | Untraced | Postoperative deaths | Number of cases treated | Clinical healing after 5 years | Died of local recurrence | Died of metastases | Died of intercurrent disease | Untraced | Postoperative deaths |
| Complete cell death | 8 | 6 | 0 | 2 | 0 | 0 | 0 | 4 | 2 | 0 | 1 | 1 | 0 | 0 |
| Questionable cell death | 4 | 2 | 0 | 1 | 0 | 1 | 0 | 4 | 2 | 0 | 2 | 0 | 0 | 0 |
| Marked histopathological change | 4 | 3 | 0 | 1 | 0 | 0 | 0 | 9 | 3 | 0 | 5 | 0 | 0 | 1 |
| Moderate histopathological change | 11 | 6 | 1 | 2 | 2 | 0 | 0 | 14 | 3 | 6 | 6 | 0 | 0 | 5 |
| Total | 27 | 17 | 1 | 6 | 2 | 1 | 0 | 31 | 10 | 6 | 14 | 1 | 0 | 6 |

The same cases as shown in Table I, grouped according to the stages of disease (Stage II and III).

Table III

| Clinical Aspect of the Mammary Tumor | No. of Cases Treated | Clinical Disappearance of Tumors at End of Treatment and End of First Year | Proved by Biopsy Disappearance of Tumors | Clinical Healing after 3 Years |
|---|---|---|---|---|
| Tumor from 4 to 6 cm., movable, thickened or invaded skin, nipple retracted or not | 33 | 27 | 17 | 22 |
| Tumor over 6 cm., movable or not, thickened or invaded skin, or edema, "peau d'orange," skin nodules | 42 | 25 | 10 | 8 |
| Ulcerated tumor | 28 | 15 | 10 | 7 |
| Extensive scirrhus, ulcerated or not, fixed to depth | 9 | 7 | 3 | 2 |
| Acute inflammatory tumor | 5 | 1 | 0 | 0 |
| Distant metastases (skin, lungs, bones). Tumor immediately bilateral | 13 | 4 | 2 | 2 |
| Total | 130 | 79 | 42 | 41 |

Showing local results (apparent clinical disappearance of the mammary tumor) at the end of the treatment, one and three years after the end of this treatment, for 130 mammary carcinomas (Stages II to IV) irradiated during the period from 1936 to 1945.

us if we are justified in continuing this type of treatment.

In the second part of the paper, we will report the statistical studies, stage by stage.

### CLASSIFICATION OF MAMMARY TUMORS

The following factors are taken into consideration:

1. Volume (less than 6 cm., and greater than 6 cm., in diameter).
2. Skin invasion.
3. Skin edema.
4. Peau d'orange.
5. Skin nodules.
6. Ulceration.
7. Inflammatory carcinoma.
8. Scirrhous carcinoma (this is placed in a separate group).

The stages of carcinoma of the breast which are considered in this paper are Stages II, III and IV. For the purposes of evaluation of the statistical tables shown later in the paper, we will now state the lesions included in the various stages:

Stage II—tumors up to 6 cm. in diameter.
—thickened or invaded skin.
—nipple retracted or not.

Stage III—Tumors over 6 cm. in diameter.
—edema, peau d'orange, skin nodules.
—ulcerated tumors.
—scirrhus
—extensive
—ulcerated or not
—fixed to deep tissues.

Stage IV—distant metastases
—inflammatory carcinoma

Note: We are also considering in a special group and eliminating from the statistics, cases up to 3 cm. in diameter (Stage I, 10 cases), where a surgical biopsy removed the small tumor (by microscopic proof).

### BEHAVIOR OF THE MAMMARY TUMOR AND THE LYMPH NODES

1. The mammary tumor.

Table III summarizes the results of 130 cases from 1936 to 1945.

Clinical disappearance was obtained after one year in 79 cases, of which 42 had been biopsied (surgical biopsy).

At the end of the third year the number of locally healed patients, living and symptom free, is 41.

Table IV shows the condition of 52 patients at the end of the fifth year (1936–1942), in Stages II, III and IV. Clinical disappearance of the tumor was obtained in 9 cases. Only 2 local recurrences have been noted during the third and fourth years, one in a Stage II case and the other

TABLE IV

| Clinical Aspect of the Mammary Tumor | No. of Cases Treated | Clinical Disappearance of Tumors at End of Treatment and End of First Year | Proved by Biopsy Disappearance of Tumors | Clinical Healing after 5 Years |
|---|---|---|---|---|
| Tumor from 4 to 6 cm., movable, thickened or invaded skin, nipple retracted or not | 10 | 6 | 1 | 4 |
| Tumor over 6 cm., movable or not, thickened or invaded skin, or edema, "peau d'orange," skin nodules | 18 | 8 | 1 | 2 |
| Ulcerated tumor | 13 | 5 | 4 | 2 |
| Extensive scirrhus, ulcerated or not, fixed to deep tissues | 4 | 3 | 1 | 0 |
| Inflammatory carcinoma | 3 | 1 | 0 | 0 |
| Distant metastases (skin, lungs, bones). Tumor initially bilateral | 4 | 2 | 0 | 1 |
| Total | 52 | 25 | 7 | 9 |

Local conditions of irradiated breasts after *five years* in 52 patients treated from 1936 to 1942 (Stages II to IV). The number of biopsies concerns only the tumors which clinically disappeared. The diminution of the number of survivals is due, chiefly, to distant metastases.

in a Stage III case. The deaths are due chiefly to the appearance of distant metastases outside the irradiated region. However, it is not possible to draw definite conclusions, because the number of these patients is too small, and among the patients dead from metastases and untraced, there may be tumors not histopathologically sterilized, but which had no opportunity of recurring clinically as the patients died too soon.

Table V shows the fate of the 130 cases during the second and third years.

2. The axillary lymph nodes.

In these, complete disappearance is more difficult to obtain.

Grouping these lymph nodes according to size, Table VI shows that in 52 cases with lymph nodes from 3 to 5 cm. in size, 26 disappeared at the end of treatment and 10 remained absent for three to five years following.

It must be noted that these lymph nodes, as well as the supraclavicular ones, have not been histopathologically proved to contain malignant cells.

3. The supraclavicular lymph nodes.

Table VII shows the results of treatment

TABLE V

| | Stage II | | Stage III | | Stage IV | |
|---|---|---|---|---|---|---|
| No. of cases treated | 33 | | 79 | | 18 | |
| Clinical disappearance verified after 1 year | 27 | −5 | 47 | −29 | 5 | −3 |
| Clinical disappearance verified after 3 years | 22 | | 18 | | 2 | |
| Died of local recurrence | 1 | +5 | 1 | +29 | 0 | |
| Died of distant metastases | 4 | | 17 | | 1 | +3 |
| Untraced | 0 | | 7 | | 1 | |
| Died of intercurrent disease | 0 | | 4 | | 1 | |

here. The survival rate diminishes considerably in the year following irradiation, not because of supraclavicular recurrence, but due to distant metastases, especially in the cases where the nodes were initially large.

### STATISTICAL STUDIES

After having considered the individual behavior of the mammary, axillary and supraclavicular tumors, we present the statistics as five year results, the patients being grouped in Stages II, III and IV (Table VIII).

Of 52 patients treated from 1936 to 1942, 8 are living after five years without any clinical evidence of cancer locally or at a distance. Four of these tumors had initial biopsies. Twenty-four distant metastases may be noted, a very high rate.

Table IX is not statistical, but shows only the local condition of the breast at the end of the third year. Of 130 patients, 41 are living and symptom free; 47 distant metastases are noted.

There are 10 Stage I tumors; the tumor was irradiated locally and completely *after a biopsy*. Nine of these patients are locally healed and symptom free after a period of three to five years. No case of local recurrence was noted, but one death from rapid metastasis occurred, the patient dying from massive liver metastasis only two months following treatment.

TABLE VI

AXILLARY LYMPH NODES

| Size of Lymph Nodes | No. of Cases Treated | Clinical Disappearance at the End of Treatment | Clinical Disappearance Verified after 3 to 5 Years |
|---|---|---|---|
| 0 cm. | 40 | | |
| 0.5 cm. | 19 | | |
| 1–2 cm. | 34 | | |
| 3–5 cm. | 52 | 26 | 10 |

Behavior of the axillary lymph nodes in 145 patients irradiated from 1936 to 1945. Only the lymph nodes (without biopsy) appearing clinically malignant and with a volume of more than 2 cm. are counted. The apparent clinical disappearance of lymph nodes under this volume (from 0.5 to 2 cm.) was obtained in a greater percentage, but these lymph nodes are eliminated from this study because they are clinically doubtful. Thus we attempt to compensate for the absence of biopsy by using more strict clinical criteria.

### TECHNICAL CONSIDERATIONS

The technique is similar to that used for other cancers, namely, 180 kv.; filter 1 mm. of copper; target skin distance 60 cm.; intensity 20 r per minute. More important is the planning of the fields, dose per treatment, total dose, and fractionation.

Fields: The average number of fields is six to seven, and the size varies from 10 by 10 cm. to 12 by 10 cm., the size being reduced near the end of the treatment when the dosage becomes high. Overlapping must be avoided, and this is made possible by marking three landmarks on

TABLE VII

SUPRACLAVICULAR LYMPH NODES

| Size of Lymph Nodes | No. of Cases Treated | Clinical Disappearance at the End of Treatment | Clinical Disappearance Verified after 1 Year | Clinical Disappearance Verified after 5 Years |
|---|---|---|---|---|
| 0.5–1 cm. | 21 | 11 | 4 | 2 |
| 1.5–3 cm. | 20 | 9* | 2 | 1 |
| 3 –7 cm | 16 | 5* | 1 | 0 |

Behavior of the supraclavicular lymph nodes. This table includes the patients treated by roentgen therapy alone, and the postoperative recurrences grouped together. We added to this table postoperative recurrences with clinically evident supraclavicular lymph nodes to increase the number of studied cases. Out of 14 cases (9*+5*) with lymph nodes larger than 1 cm., 7 were non-operated patients and 7 were postoperative recurrences. The diminution of the number of survivals noted after the first year is due. not to a supraclavicular recurrence, but to distant metastases.

TABLE VIII

| | Without Lymph Nodes | | | | Axillary Lymph Nodes | | | | Supraclavicular Lymph Nodes | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases treated | Apparent healing after 5 years | Proved by biopsy disappearance of tumors | Died of distant metastases | Cases treated | Apparent healing after 5 years | Proved by biopsy disappearance of tumors | Died of distant metastases | Cases treated | Apparent healing after 5 years | Proved by biopsy disappearance of tumors | Died of distant metastases | Cases treated | Apparent healing after 5 years | Proved by biopsy disappearance of tumors | Died of distant metastases |
| Tumor from 4 to 6 cm., movable thickened or invaded skin nipple retracted or not | 5 | 2 | 0 | 2 | 5 | 2 | 1 | 1 | | | | | 10 | 4 | 1 | 3 |
| Tumor over 6 cm., movable or not; skin thickened or invaded | 3 | 1 | 1 | 1 | 5 | 0 | 0 | 4 | 1 | 0 | 0 | 1 | 9 | 1 | 1 | 6 |
| Tumor over 6 cm., edema, "peau d'orange," skin nodules | | | | | 9 | 0 | 0 | 5 | | | | | 9 | 0 | 0 | 5 |
| Ulcerated tumor | 5 | 1 | 1 | 0 | 7 | 1 | 1 | 3 | 1 | 0 | 0 | 1 | 13 | 2 | 2 | 4 |
| Extensive scirrhus, ulcerated or not, fixed to deep tissues | | | | | 3 | 0 | 0 | 1 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 1 |
| Inflammatory carcinoma | | | | | 3 | 0 | 0 | 2 | | | | | 3 | 0 | 0 | 2 |
| Distant metastases (skin, lungs, bones), tumor initially bilateral | | | | | 4 | 1 | 0 | 3 | | | | | 4 | 1 | 0 | 3 |
| Total | 13 | 4 | 2 | 3 | 36 | 4 | 2 | 19 | 3 | | | | 52 | 8 | 4 | 24 |

Statistical studies of 52 patients (Stages II, III, IV), treated by roentgen therapy alone (*five year results*). The patients are grouped according to the clinical aspect of the breast tumor and the axillary and supraclavicular lymph nodes. Note the frequency of metastasis which gets higher with the increasing invasion of axillary and supraclavicular lymphatics. The biopsies noted concern exclusively the tumors which disappeared.

To simplify the table, the patients untraced or dead from intercurrent disease are not counted here, but only distant metastases.

TABLE IX

| | Without Lymph Nodes | | | | Axillary Lymph Nodes | | | | Supraclavicular Lymph Nodes | | | | Total | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases treated | Apparent healing after 3 years | Proved by biopsy disappearance of tumors | Died of distant metastases | Cases treated | Apparent healing after 3 years | Proved by biopsy disappearance of tumors | Died of distant metastases | Cases treated | Apparent healing after 3 years | Proved by biopsy disappearance of tumors | Died of distant metastases | Cases treated | Apparent healing after 3 years | Proved by biopsy disappearance of tumors | Died of distant metastases |
| Tumor 4 to 6 cm., movable, thickened or invaded skin (nipple retracted or not) | 12 | 8 | 2 | 2 | 21 | 14 | 12 | 4 | | | | | 33 | 22 | 14 | 6 |
| Tumor over 6 cm. (movable or not), skin thickened or invaded | 5 | 3 | 2 | 1 | 22 | 3 | 1 | 11 | 2 | 0 | 0 | 1 | 29 | 6 | 3 | 13 |
| Tumor over 6 cm., edema, "peau d'orange," skin nodules | | | | | 13 | 2 | 2 | 6 | | | | | 13 | 2 | 2 | 6 |
| Ulcerated tumor | 5 | 1 | 1 | 1 | 21 | 6 | 4 | 6 | 2 | 0 | 0 | 1 | 28 | 7 | 5 | 8 |
| Extensive scirrhus ulcerated or not; fixed to deep tissues | 3 | 1 | 1 | 1 | 5 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 9 | 2 | 2 | 2 |
| Inflammatory carcinoma | | | | | 4 | 0 | 0 | 2 | 1 | 0 | 0 | 1 | 5 | 0 | 0 | 3 |
| Distant metastases (skin, lungs, bones), tumor initially bilateral | | | | | 9 | 2 | 2 | 6 | 4 | 0 | 0 | 3 | 13 | 2 | 2 | 9 |
| Total | 25 | 13 | 6 | 5 | 95 | 28 | 222 | 36 | 10 | 0 | 0 | 5 | 130 | 41 | 28 | 47 |

Local conditions of 130 patients (Stages II, III, IV) treated by roentgen therapy alone (*three year results*). The patients are grouped according to the clinical aspect of the breast tumor and the axillary and supraclavicular lymph nodes. Note the frequency of metastasis which increases with the increasing invasion of axillary and supraclavicular lymphatics. The biopsies noted concern exclusively the tumors which disappeared.

To simplify the table, the patients untraced or dead from intercurrent disease are not counted here, but only distant metastases.

TABLE X

| Tumor Dose (Mid-point of Breast) in Roentgens | Tumor 4 to 6 cm., Movable Thickened or Invaded Skin, Nipple Retracted or Not | | | Tumor over 6 cm., Movable or Not, Thickened or Invaded Skin, or Edema, "Peau d'orange," Skin Nodules | | | Ulcerated Tumor | | | Extensive Scirrhus, Ulcerated or not, Fixed to Deep Tissues | | | Inflammatory Carcinoma | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases treated | Disappearance of tumors at end of treatment | Proved by biopsy | Cases treated | Disappearance of tumors at end of treatment | Proved by biopsy | Cases treated | Disappearance of tumors at end of treatment | Proved by biopsy | Cases treated | Disappearance of tumors at end of treatment | Proved by biopsy | Cases treated | Disappearance of tumors at end of treatment | Proved by biopsy |
| 4,100 | 3 | 3 | 0 | | | | 1 | 0 | 1 | | | | | | |
| 4,500 to 5,000 | 1 | 0 | 0 | 8 | 2 | 1 | 4 | 0 | 3 | 1 | 0 | 1 | 1 | 0 | 0 |
| 6,000 to 6,800 | 7 | 6 | 5 | 14 | 9 | 3 | 6 | 3 | 4 | 3 | 2 | 1 | 1 | 1 | 0 |
| 7,000 to 8,000 | 14 | 12 | 7 | 11 | 6 | 4 | 2 | 2 | 1 | 2 | 2 | 1 | 3 | 0 | 0 |
| 9,000 | 4 | 3 | 3 | 5 | 4 | 3 | 8 | 5 | 5 | 1 | 1 | 1 | | | |
| over 9,000 | 4 | 3 | 3 | 4 | 4 | 2 | 7 | 5 | 6 | 2 | 2 | 2 | | | |
| Total | 33 | 27 | 18 | 42 | 25 | 13 | 28 | 15 | 20 | 9 | 7 | 6 | 5 | 1 | 0 |

Showing the approximate tumor dose, evaluated in the center of the breast applied through two mammary fields right and left apposing. The apparent clinical disappearance of the tumor in these cases has been noted one year at least after the treatment. We noticed that this clinical disappearance is obtained, in a significant proportion, only after a dose of about 5,000 r.

Number of irradiated patients: 117. Not considered in this table: 18 patients of Stage I and Stage IV.

TABLE XI

| Clinical Aspect of the Mammary Tumor | 4 to 6 Weeks | | | 6 to 8 Weeks | | | 8 to 10 Weeks | | | 10 to 11 Weeks | | | 11 to 12 Weeks | | | 12 to 14 Weeks | | | 14 Weeks and More | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Cases treated | Clinically Well | | Cases treated | Clinically Well | | Cases treated | Clinically Well | | Cases treated | Clinically Well | | Cases treated | Clinically Well | | Cases treated | Clinically Well | | Cases treated | Clinically Well | |
| | | After 3 years | Proved by biopsy | | After 3 years | Proved by biopsy | | After 3 years | Proved by biopsy | | After 3 years | Proved by biopsy | | After 3 years | Proved by biopsy | | After 3 years | Proved by biopsy | | After 3 years | Proved by biopsy |
| Tumor from 4 to 6 cm., movable, thickened or invaded skin (nipple retracted or not) | 5 | 3 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 6 | 4 | 4 | 9 | 5 | 4 | 4 | 1 | 1 | 8 | 8 | 6 |
| Tumor over 6 cm. (movable or not), thickened or invaded skin, or edema, "peau d'orange," skin nodules | | | | 5 | 0 | 0 | 5 | 0 | 0 | 1 | 0 | 0 | 7 | 3 | 2 | 15 | 4 | 2 | 9 | 1 | 1 |
| Ulcerated tumor | 1 | 0 | 0 | 1 | 0 | 0 | | | | 4 | 0 | 0 | 5 | 2 | 1 | 6 | 1 | 1 | 11 | 4 | 3 |
| Extensive scirrhus (ulcerated or not) fixed to deep tissues | 1 | 0 | 0 | | | | | | | 3 | 0 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 3 | 1 | 1 |
| Inflammatory carcinoma | | | | | | | | | | | | | | | | 3 | 0 | 0 | 2 | 0 | 0 |
| Distant metastases (skin, lungs, bones), tumor initially bilateral | | | | 1 | 0 | 0 | 1 | 0 | 0 | | | | 1 | 0 | 0 | 6 | 2 | 0 | 4 | 0 | 0 |
| Total | 7 | 3 | 0 | 7 | 0 | 0 | 7 | 1 | 0 | 14 | 4 | 4 | 23 | 10 | 7 | 35 | 9 | 5 | 37 | 14 | 11 |

Showing the results of various methods of fractionation in 130 breast carcinomas (Stages II to IV); three year results (1936 to 1945). It is imperative to use the fractionation method to avoid accidents. The treatment period increases with the given dose. In our present policy, the lower limit of this fractionating is *three months*.

the skin at the confluence of fields (see Fig. 2, 3 and 4). The two mammary fields

FIG. 2

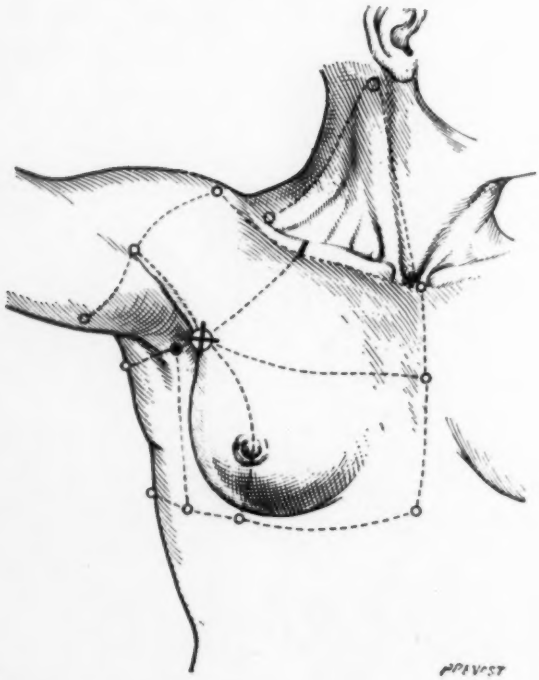


FIG. 3

must be applied tangentially to the chest wall, and directly opposing; if the breast is very large, a third mammary field is applied as a direct anterior field. Irradiation must be applied following a rhythmical alteration with an interval of two to three days between successive treatments to any one field.

Total dose: The tumor dose has been evaluated in Table x for 117 patients (three year results).

It is seen from Table x that local clinical disappearance becomes more frequent after a tumor dose of 6,000 to 6,800 r.

The tumor dose in the axillary lymph nodes varied from 6,000 to 7,000 r in the

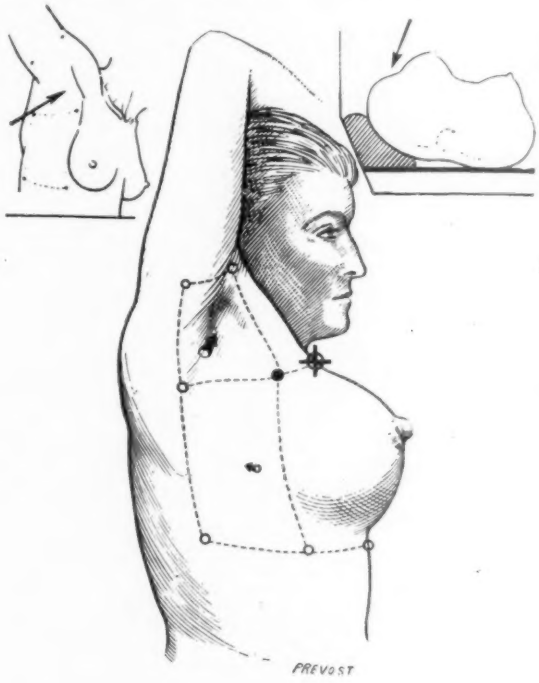


FIG. 4

lymph nodes which disappeared clinically.

The skin dose for the supraclavicular nodes is at least 4,500 to 5,200 r (4,100 r in one case only).

It must be remembered that this is only the clinical disappearance of the tumor that we are considering, and we emphasize that it is not possible to say if the mammary tumor and the lymph nodes have histopathologically disappeared after this short time of three years.

These very high doses are only advisable with protracted fractionation.

Fractionation: Table XI shows the fractionation for 130 cases (Stage II, III and IV) (five year result at least).

The fractionation is increased with increasing total doses, which themselves vary with the extent and size of the mammary tumor and of the lymph nodes.

Treatment is usually fractionated over three months, and over four months in the intensive and radioresistant lesions.

For the supraclavicular region, one field is used; the average fractionation period is three months, for the doses indicated previously. This is the only way to avoid late skin changes. The daily dose per field varies from 200 to 250 r, in exceptional cases (and temporarily only) 300 r per field (skin dose). Two fields are treated daily—rarely three (and only temporarily), when the patient is obese and in good general health.

## COMPLICATIONS

These vary according to the dose administered and the fields utilized. The tissues affected are skin, subcutaneous tisues, muscles and nerves, bones (fractures), lungs and heart. They are due to obvious mistakes, because of too high doses, too large fields (and overlapping), and faulty direction of the beam.

## SUMMARY

Roentgen therapy of the breast as here described is a treatment confined exclusively to the breast and regional lymphatic areas. It is concerned only with the clinical disappearance of the mammary tumor and the lymph nodes after periods of three to five years following treatment. It does not deal with the treatment of distant metastases which remains a separate problem and is not discussed here.

The patients reported here with a mammary tumor or axillary or supraclavicular nodes clinically disappeared, are patients living at this time, three to five years at least after the treatment, without evidence of distant metastases, and symptom free.

The patients dead from distant metastases are counted as failures even when the mammary tumor and lymph nodes had disappeared completely at the time of death.*

Fondation Curie
Paris, France

* For discussion see page 349.

# TREATMENT AND RESULTS IN CANCER OF THE BREAST*

*By* ELIS BERVEN, M.D.
*Professor of Radiotherapy, University of Stockholm; Director of Radiumhemmet*
STOCKHOLM, SWEDEN

AT Radiumhemmet all cases of cancer of the breast are clinically examined not only by an experienced surgeon but also by at least two radiotherapists. These three specialists class a given case, on the basis of their clinical findings, according to the three stages suggested by Steinthal. Nevertheless, our experience at Radiumhemmet has shown that in 15 per cent of the cases which had clinically been classed Stage I (Steinthal), the microscopic examination disclosed that they were Stage II cases. In addition, the microscopic examination showed in almost one-third of these cases that the tumor had grown through the capsule of the lymph node. The latter condition is, in the light of prognosis, a very unfavorable sign, which the clinical examination fails to reveal.

Also in about 30 per cent of the cases which are clinically classed Stage II the microscopic examination of the axillary lymph nodes showed that they were Stage I cases. The percentage of this incorrect classification published in the literature is, as a rule, much higher.

If the classification of cases of cancer of the breast is based only on clinical findings the results of radiation treatment of cancer of the breast published by different clinics are statistically not comparable. A classification according to Steinthal therefore cannot be used as a basis for comparative statistical studies. The staging of cancers of the breast must be based on the findings of a careful microscopic examination of all axillary lymph nodes.

Apart from metastasis to the axilla, other symptoms such as fixation to the skin or ulceration of the tumor have a comparatively insignificant bearing on prognosis.

Since 1921 we have largely been using the same methods at Radiumhemmet; namely, either only postoperative or preoperative and postoperative roentgen treatment.

The patients treated at Radiumhemmet are referred either from general County Hospitals in the North of Sweden and Mid-Sweden, or from the Karolinska Hospital in Stockholm, the surgical mother-clinic of Radiumhemmet. From the clinical point of view, these cases vary widely. From the Karolinska Hospital all operable cases are referred no matter in which stage they are clinically.

From the County Hospitals, however, only about 60 per cent of the operable cases are referred for radiation treatment. The reason for this is that the surgeons-in-chief in these hospitals do not refer early cases which in their opinion are in Stage I (Steinthal) for preoperative treatment, because they feel that surgical treatment alone yields fully satisfactory results in such cases. If, however, in these cases there is microscopic evidence of metastases to the axillary nodes, the patients are referred for postoperative treatment. Hence in the light of prognosis the cases referred to Radiumhemmet from these hospitals are rather bad, far-advanced cases.

On the other hand, for primary preoperative treatment, only such patients are usually referred in whom metastases to the axillary nodes were clinically demonstrable or who surgically were borderline cases. Hence, also the cases sent to Radiumhemmet from the County Hospitals for preoperative treatment are, as regards prognosis, fairly unfavorable cases.

In preoperative treatment roentgen rays are given to a large anterior field (20 by 30

* Presented in a Panel Discussion on Treatment and Results in Cancer of the Breast at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

cm.), including the breast, axilla and the supraclavicular fossa. The breast is lifted up and fixed with sandbags in the axilla. In addition, treatment is given through a posterior field (10 by 15 cm.), covering the breast (still fixed in the axilla) and the axilla. We give nowadays to each field 350 r each time, five times using 180 kv., 0.5 mm. Cu filter, 50 cm. target-skin distance; the total tumor dose given over ten days is approximately 2,000 r, that given to the axilla, approximately 1,500 r.

If the breast is small and if the tumor is localized to the medial part of the breast, four portals are used, namely a medial and a lateral to the breast, and an anterior and a posterior, including the axilla.

Although this dosage produces a mild erythema of the skin it does not affect the healing process after operation. The operation is performed three weeks after the end of the treatment.

As soon as the surgical wound is healed the first postoperative treatment is given using two fields, i.e. a large anterior field including the operated area and the supraclavicular fossa and a posterior field including the axilla and the supraclavicular fossa. To the anterior field we give 300 r each time, three times using 102 kv., 1 mm. Al filter, 50 cm. target-skin distance. To the posterior field we give 3×350 r, 0.5 mm. Cu plus 1 mm. Al, distance 40–50 cm. After two months this treatment is repeated, and after another three months a third course of postoperative treatment is given with the same technique. This dosage is also used in cases in which the patients receive postoperative treatment only.

This technique is modified according to the type of the case and the microscopic findings. In later years, we have, in cases where the tumor is localized to the medial part of the breast, treated the mediastinum. To women at the reproductive age we give in addition a castration dose to the ovaries.

Recurrences in the skin of the operation field are rare, as seen in Table 1.

Skin recurrences have developed in 88 of 802 cases, or in 10 per cent. Only 26, or 3 per cent, are real skin local recurrences as in 52 cases the skin recurrence was a part of the generalized metastases.

In some cases where the tumor was highly radiosensitive and classed Stage II we have prophylactically also treated the spine and the pelvic bones.

In Sweden the criteria for operation are less rigid than in the United States. We consider only those cases inoperable where the tumor is fixed to the thoracic wall and where there is evidence of either massive and fixed metastases to the axillary lymph nodes or to the supraclavicular fossa or to distant organs. Fixation to the skin or ulceration of the tumor is no contraindication to operation if preoperative roentgen treatment has been given. Neither are pregnancy, lactation and the inflammatory type of carcinoma. In pregnant women pregnancy is interrupted.

Table I

RECURRENCES IN THE SKIN OF THE OPERATION FIELD

| | No. of Cases | No. of Cases with Local Recurrences |
|---|---|---|
| Stage I | 298 | 21 or 7% |
| Stage II | 471 | 52 or 11% |
| Stage III | 33 | 5 or 15% |
| Total | 802 | 88 or 10% |

Skin recurrences have developed in 88 of 802 cases, or in 10 per cent. Only 26, or 3 per cent, are real local skin recurrences as in 52 cases the skin recurrence was a part of the generalized metastases.

In Table II the 3,623 cases observed at Radiumhemmet during the period covering the years from 1921 to 1941 are compiled.

1,164 cases have had preoperative and postoperative treatment.

640 only postoperative treatment.

535 cases with recurrences after operation at other clinics have had different types of radiation treatment.

544 cases were inoperable on admission, and have had palliative treatment only.
Inoperable cases, which became operable after treatment are included in the pre- and postoperatively treated series.

740 cases were too advanced for treatment.

The comparatively small number of cases of recurrence and of cases at a very

TABLE II

FIVE YEAR RESULTS IN 3,623 CASES OF BREAST CARCINOMA OBSERVED AT RADIUMHEMMET 1921–1941
ALL DEAD CASES ARE COUNTED AS DEAD OF CANCER

| | | No. of Cases | Well | | Survivals | |
|---|---|---|---|---|---|---|
| Pre-and postoperative treatment | Period 1921–1935 | 607 | 251 | 41% | 269 | 44% |
| Microscopic Stages I and II | Period 1936–1941 | 557 | 240 | 43% | 286 | 51% |
| | Total | 1,164 | | | | |
| Postoperative treatment only | Period 1921–1935 | 428 | 186 | 43% | 202 | 47% |
| Clinical Stages I and II | (only 285 micr. verified and classified) | | | | | |
| Microscopic Stages I and II | Period 1936–1941 | 212 | 93 | 44% | 105 | 50% |
| | Total | 640 | | | | |
| Total of cases treated by radiation and operated on | Period 1921–1935 | 1,035 | 437 | 42% | 471 | 46% |
| | Period 1936–1941 | 769 | 333 | 43% | 391 | 51% |
| | Total | 1,804 | | | | |
| Radiation treated recurrences after operation | Period 1921–1935 | 417 | 40 | 9% | 47 | 11% |
| | Period 1936–1941 | 118 | — | — | 15 | 13% |
| | Total | 535 | | | | |
| Treated Inoperable cases | Period 1921–1935 | 363 | — | — | 32 | 9% |
| | Period 1936–1941 | 181 | — | — | 5 | 3% |
| | Total | 544 | | | | |
| Cases too advanced for treatment | Period 1921–1935 | 635 | — | — | — | — |
| | Period 1936–1941 | 105 | — | — | — | — |
| | Total | 740 | | | | |

advanced stage during the years 1936–1941 is due to the fact that in the majority of these hopeless cases the patients are now offered facilities for palliative roentgen treatment in the County Hospitals.

I shall confine myself to a discussion of the results in operable radiation treated cases during the two periods 1921–1935 and 1936–1941.

Only approximately 40 per cent of the operable cases are found to be in Stage I, 60 per cent in Stage II.

Unfortunately this proportion between these two stages has not improved in the past twenty-one years despite the ever-increasing propaganda to seek medical advice as early as possible.

In Sweden as many as approximately 50 per cent of all breast cancers are found to be inoperable when first seen. During the first period 1921–1935, there were 1,035 cases treated (143 of them, operated upon on clinical findings without microscopic confirmation, were postoperatively treated). The five year cure rate was 42 per cent and the survival rate 46 per cent. In the second period there is a slight improvement in the results, the five year cure rate being 43 per cent and the survival rate 57 per cent (Table II).

The results in the different periods of the preoperative and postoperative and only postoperative cases in Stages I and II microscopically verified are compiled in Table III.

I will first discuss the results in the preoperatively and postoperatively treated cases. In the fifteen year period 1921–1935, 607 cases were treated, in the six year period 1936–1941, 557 cases. In Stage I in the first period (216 cases) the five year cure rate is 71 per cent and the survival rate 72 per cent.

The corresponding numbers in the second period are 60 per cent and 66 per cent. The lower healing percentage in the second period is probably due to the fact that during this period cases, inoperable on admission, have become operable and have been operated upon.

In Stage II (391 patients from 1921–1935 and 354 from 1936–1941) the five year cure rate has risen from 24 per cent in the first period to 34 per cent in the second and the survival rate from 28 per cent to 43 per cent, a marked improvement.

In the postoperatively radiation treated cases it is not possible to compare the results from the different periods, since in the period 1921–1935 only in two-thirds was there microscopic evidence in support of both the diagnosis and the classification. In the whole group the five year cure has risen from 40 per cent to 44 per cent and the survival rate from 44 per cent to 50 per cent.

A reliable comparison between the results in the preoperatively and postoperatively and only postoperatively treated cases is possible in the series from 1936–1941. In Stage I there is no difference in the survival rates between the preoperatively and postoperatively and the postoperatively only treated cases (66 per cent).

In Stage II, in contrast, the survival rate

TABLE III

CANCER OF THE BREAST

Five year results in microscopically verified Stages I and II

| Stages | Pre- and Postoperative Roentgen Treatment | No. of Cases | Five Year Results | | | |
|---|---|---|---|---|---|---|
| | | | Well | | Survivals | |
| I | Period 1921–1935 | 216 | 155 | 71% | 157 | 72% |
| II | Period 1921–1935 | 391 | 96 | 24% | 112 | 28% |
| | Total | 607 | 251 | 41% | 269 | 44% |
| I | Period 1936–1941 | 203 | 121 | 60% | 135 | 66% |
| II | Period 1936–1941 | 354 | 120 | 34% | 151 | 43% |
| | Total | 557 | 241 | 43% | 286 | 51% |
| | Postoperative Roentgen Treatment Only | | | | | |
| I+II | Period 1921–1935 verified but not classified cases | 285 | 115 | 40% | 126 | 44% |
| I | Period 1936–1941 | 95 | 58 | 61% | 63 | 66% |
| II | Period 1936–1941 | 117 | 35 | 30% | 42 | 36% |
| | Total | 212 | 93 | 44% | 105 | 50% |

TABLE IV

THE 451 CASES IN STAGE II (1936–1941) DIVIDED INTO THREE GROUPS ACCORDING TO THE EXTENT OF AXILLARY METASTASES

| | Postoperative Roentgen Treatment | | | Pre- and Postoperative Roentgen Treatment | | |
|---|---|---|---|---|---|---|
| | No. of Cases | Survivals | | No. of Cases | Survivals | |
| Group I (metastasis to one node) | 18 | 13 | 72% | 79 | 57 | 72% |
| Group II (metastases to several nodes) | 69 | 27 | 39% | 164 | 62 | 38% |
| Group III (periglandular infiltration in the axilla) | 30 | 2 | 7% | 91 | 29 | 37% |

is 43 per cent in the preoperative and postoperative cases and 36 per cent in the postoperative, an improvement which is not statistically fully significant, but indicates the importance of the preoperative treatment

Stronger evidence for this is given in the compilation in Table IV.

Stage II can be divided into the following three groups:

Group I Cases with microscopically verified metastases to one lymph node.

Group II Cases with metastases to two or more lymph nodes.

Group III Cases where the tumor has grown through the capsule and infiltrates the connective and fatty tissue.

The survival rate in both Group I and II is approximately the same whether preoperative and postoperative radiation treatment was given or only postoperative treatment (Table IV).

In Group III, however, the survival rate in 30 patients who had been given solely postoperative radiation treatment is 6.7 per cent. In 91 patients who had been given both preoperative and postoperative radiation treatment, it is 31.9 per cent, a statistically significant improvement.

These findings strongly support the assumption that preoperative roentgen treatment greatly improves the prognosis in cases where the cancerous growth has begun to invade the axillary tissue.

It cannot be sufficiently emphasized that it is not possible clinically to determine whether the growth is in Stage I or II. It is therefore imperative that all cases should be given preoperative roentgen treatment.

On comparing the results of the treatment in patients referred to us from different County Hospitals against those in patients referred to us from Karolinska Hospital interesting facts are revealed (Table V).

In the former group the survival rate in

TABLE V

FIVE YEAR RESULTS IN CASES OF CANCER OF THE BREAST TREATED BY ROENTGEN RADIATION PREOPERATIVELY AND POSTOPERATIVELY OR SOLELY POSTOPERATIVELY; 387 CASES REFERRED FROM THE SURGICAL MOTHER-CLINIC OF RADIUMHEMMET AND 298 REFERRED FROM COUNTY HOSPITALS

| | Stages | No. of Cases | Survivals | |
|---|---|---|---|---|
| | | | Cases | Per Cent |
| Karolinska Hospital | I | 133 | 107 | 80 |
| | II | 254 | 111 | 45 |
| County Hospitals | I | 165 | 90 | 55 |
| | II | 217 | 82 | 38 |

Stage I is 55 per cent and in the latter 80.4 per cent. In Stage II in the former it is 38 per cent and in the latter 45 per cent.

The healing percentage in the group from Karolinska Hospital is the most accurate expression of the prognosis in operable cases of cancer of the breast.*

Radiumhemmet
Stockholm, Sweden

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* For discussion see page 349.

# TREATMENT AND RESULTS IN CANCER OF THE BREAST*

*By* SIR STANFORD CADE, K.B.E., C.B., F.R.C.S.
*Surgeon, Westminster Hospital, Mount Vernon Hospital and the Radium Institute*
LONDON, ENGLAND

SUCCESS or failure in treatment of cancer of the breast depends mainly on two factors: (1) the stage of the disease when treatment is undertaken; (2) the quality of the treatment. These two factors will be considered separately and in their relation to each other.

## STAGE OF THE DISEASE

With minor modifications, U. V. Portmann's classification has been adopted. It is as follows.

Stage I Tumor of the breast only.
Stage II Tumor of the breast plus skin changes and/or axillary lymph nodes.
Stage III Tumor of the breast plus supraclavicular lymph nodes or contralateral axillary lymph nodes or fixation to pectoral fascia.
Stage IV Skeletal or visceral metastasis.

This staging is a clinical one, as it must be, if the choice of method of treatment and technique are to be based on it. Amplification of the significance of the staging is of importance. It is admitted that not all axillary lymph nodes containing metastasis are clinically palpable; conversely a few palpable axillary nodes prove subsequently to be free from metastasis. But if Stage I is a strictly clinical stage, it is limited to the earliest cases with the best prognosis, providing the best treatment is given.

Stage II includes various types of skin involvement. These can be subdivided into three main groups: (1) When the tumor is adherent to the overlying skin; this group varies from mere puckering of the skin over the tumor to fungation through the skin, but at both extremes it is a direct spread of the tumor outwards. (2) When the skin is edematous, the "peau d'orange" or pig-skin type; it indicates lymphatic blockage and spread of disease by lymphatic invasion; it is a much graver clinical sign than direct spread. (3) The discrete skin nodules; these vary from one or two to numerous and widespread distribution of nodules. It is an indication that the disease has metastasized widely and is quite unsuitable for any form of surgical treatment.

Stage III includes the patient with supraclavicular or contralateral lymph nodes. This indicates that the disease is outside the anatomical field covered by radical mastectomy. Stage III also includes cases where the tumor is fixed to the pectoral fascia and hence beyond surgery.

## QUALITY OF TREATMENT

There are two main therapeutic measures, surgery and radiotherapy. The general principles of surgery in cancer must be applied to the surgical treatment of breast cancer. These principles are well known and need not be reiterated here; these principles dictate the performance of a radical mastectomy. Simple mastectomy is unsound and only justifiable as a palliative measure in a small group of cases, where radical mastectomy is not indicated. Simple mastectomy by itself very seldom cures the patient. It leaves untouched the very site which determines the patient's future—axillary nodes.

*Radiotherapy*. Both radium and roentgen rays can be used with success. The technique of roentgen irradiation is simpler and more convenient to the patient. As practiced at Westminster Hospital it can be summarized as follows: 200–220 kv.; half-value layer 2.2 mm. copper; target skin distance 40–50 cm.; filtration 2.0 mm. of copper or Thoraeus filter. In most cases the

* Presented in a Panel Discussion on Treatment and Results in Cancer of the Breast at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

roentgen-ray beams are directed to the three sides of a triangular space in such a way that maximum uniformity of dosage is achieved throughout the volume treated; this volume includes the breast and the axilla and the chest wall on the side treated. The duration of the treatment is four to five weeks and the average total tumor dose is 3,500 roentgens.

When radium is used, either the interstitial or surface methods are employed. In the former a systematic needling of the breast, axilla and supraclavicular and infraclavicular areas is carried out. Long low intensity needles are used; a total of 75 to 100 mg. is needed and the duration of treatment is seven days continuous irradiation. With surface radiation a sorbo rubber plaque is made to fit the chest wall and the radium is distributed on it according to the Manchester distribution rules. Treatment is intermittent, twelve hours daily over a period of three to four weeks. The only advantage of radium over roentgen rays is the greater tissue dose achieved, namely 6,000 to 9,000 gamma roentgens. The majority of cases are treated by roentgen irradiation and only a few selected cases by radium.

*Choice of Method of Treatment.* The distinction of preoperative and postoperative radiotherapy is quite clear. Radiotherapy adequately given leads to clinical regression of the tumor. There is ample histopathological evidence that total disappearance of the tumor can be so achieved. It is the permanency of such regression which cannot be forecast. On common sense grounds, it is obvious that preoperative irradiation is of greater value than postoperative treatment. Further there is statistical evidence that preoperative irradiation gives improved long term results. Postoperative irradiation in Stage I cases has not improved the results achieved by radical surgery alone, namely 65 to 75 per cent of ten year survivals. The choice of treatment can be summarized as follows.

Stage I—Radical surgery.
Stage II—Preoperative radiotherapy and radical surgery.
Stage III—Radiotherapy only.

It must be emphasized that surgery in Stage III is not warranted and often leads to more rapid progress of the disease than if no treatment were given.

This review is based on a total of 915 cases of cancer of the breast treated personally since 1924; of these, 348 cases lend themselves to a fifteen year survey (Table I) and 263 cases to an analysis according to the method of treatment (Table II).*

Westminster Hospital
London, England

* For discussion see page 349.

Table I

CANCER OF THE BREAST, 348 CASES

| | Total Number | Percentage of Survivals Free from Disease | | |
|---|---|---|---|---|
| | | Years | | |
| | | 5 | 10 | 15 |
| Stage I | 97 | 87 | 65 | 36 |
| Stage II | 138 | 29 | 25 | 12 |
| Stage III | 95 | 20 | 15 | 7 |
| Stage IV | 18 | 0 | 0 | 0 |

Table II

CANCER OF THE BREAST 1932–1938: 263 CASES: 5 AND 10 YEAR SURVIVALS

| | Surgery | | Radium | | Surgery + Radium | |
|---|---|---|---|---|---|---|
| | Years | | Years | | Years | |
| | 5 | 10 | 5 | 10 | 5 | 10 |
| Stage I | 87% | 65% | 70% | 60% | 78% | 63% |
| Stage II | 29% | 25% | 25% | 21% | 35% | 32% |
| Stage III | 9% | 7% | 15% | 13% | 10% | 9% |

# THE TREATMENT AND RESULTS IN CANCER OF THE BREAST AT THE PRESBYTERIAN HOSPITAL, NEW YORK*

*By* C. D. HAAGENSEN, M.D.
NEW YORK, NEW YORK

DURING the past twenty-five years, at the Presbyterian Hospital in New York, there has been a trend toward a more radical surgical attack upon cancer of the breast. Our reliance upon irradiation for the cure of the disease has faltered, until we have come to the point where we reserve irradiation for cases in which palliation is all that can be hoped for. Looking backward, there are two factors which have led us toward more radical surgery and away from irradiation.

The first reason has to do with the fact that the Presbyterian Hospital is one of several American teaching hospitals where generous provision of facilities and funds has made the Halsted type of surgery possible. By the Halsted type of surgery we mean meticulous dissection, with exact hemostasis and gentle handling of tissues, usually with silk technique. With this type of surgery it is possible to carry out more thorough dissections in which a great deal more tissue is removed. Radical mastectomy, for instance, when done in this truly radical manner, requires between five and six hours to carry out. The fact that we have had the privilege of working in a hospital where we have been permitted to indulge a desire for thoroughness has, of course, enabled us to carry out methods which might not be practical in all hospitals.

A second factor that influenced us toward surgery rather than irradiation was our experience in an experimental series of cases in which Dr. Lenz, Dr. Stout and I attempted to destroy cancer of the breast with intensive irradiation.[8]

In a total of 38 cases treated between 1933 and 1937, intensive protracted roentgen treatment was given. Dr. Lenz has described his methods elsewhere. The fractional dose method was used, 100 to 200 roentgens being given daily to each of one or more portals. The breast was treated through four portals directed tangentially to the chest wall, and often through an additional portal directly over the tumor. The axilla and supraclavicular regions were treated through an anterior and a posterior portal and through a third axillary portal. The tumor dose to the primary lesion of the breast reached 4,500 r. Two or more months were required for the treatment. After a delay of at least another month for the severe cutaneous reaction to subside, radical mastectomy was done. In every case in the series, persisting carcinoma cells were found in the microscopical studies. Although the cancer cells were usually damaged by the irradiation, they were not all destroyed. Metastases in axillary lymph nodes seemed to be more resistant than the primary growth. The details of the histopathological findings in representative cases in the series were reported by Beach.[2] This experience discouraged us in our hope of curing cancer of the breast with irradiation and led us toward reliance solely upon surgery.

If these heroic doses of radiation fail to cure, the much smaller ones given in the usual prophylactic preoperative or postoperative irradiation would seem futile and we have therefore given up prophylactic irradiation. This failure of irradiation as a curative agent has in no way lessened our reliance upon irradiation for palliation, where it is of inestimable value.

* From the Department of Surgery of the Presbyterian Hospital, and the Laboratory of Surgical Pathology, Columbia University. Presented in a Panel Discussion on Treatment and Results in Cancer of the Breast at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

SELECTION OF CASES FOR OPERATION

When we came to realize that in our hands surgery was our sole reliance for the *cure* of cancer of the breast, we sought to improve our surgical attack. The first step in this direction was to select our patients for operation more critically.

In the Presbyterian Hospital, as in a good many others, certain surgeons had been accustomed to operate upon almost every case of cancer of the breast applying for treatment, no matter how advanced it might be, with the faint hope that cure might be achieved. From observing results of this kind of desperate surgery, we learned that patients with certain clinical forms of the disease are never cured, no matter how radical the operation. Dr. Stout and I set out to try to define, from the records of our hospital, which were exceptionally complete, just which types of cases had been cured by operation. We used the punch card method in studying our data, which made it possible to correlate the five year cure rate and the local recurrence rate with a whole series of clinical features of cancer of the breast as recorded in our series of cases. Our first study, presented in 1942,[3] included a total of 876 primary cases coming to the Presbyterian Hospital between 1915 and 1934, inclusive. In 640, or 73.1 per cent, radical mastectomy was done.

To illustrate the way in which we studied the prognostic significance of the various clinical signs of the disease, we might describe our findings as regards edema of the skin. Edema develops when the subdermal lymphatics are blocked by carcinoma emboli. This fact explains why edema is such a grave sign. Actually, we found that not a single one of 41 patients, in whom one-third or more of the skin over the breast showed edema, was cured by radical mastectomy. The local recurrence rate in these 41 patients was 66 per cent.

From our studies we worked out the following rule for judging operability in carcinoma of the breast.[4,6]

Women of all age groups who are in good enough general condition to run the risk of major surgery should be treated by radical mastectomy, except as follows: (1) when the carcinoma is one which developed during pregnancy or lactation; (2) when extensive edema of the skin over the breast is present; (3) when satellite nodules are present in the skin over the breast; (4) when intercostal or parasternal tumor nodules are present; (5) when there is edema of the arm; (6) when proved supraclavicular metastases are demonstrated; (7) when the carcinoma is the inflammatory type; (8) when distant metastases are demonstrated; (9) when any two, or more, of the following signs of locally advanced carcinoma are present: (a) ulceration of the skin; (b) edema of the skin of limited extent (less than one-third of the skin over the breast involved); (c) solid fixation of the tumor to the chest wall; (d) axillary lymph nodes measuring 2.5 cm. or more, in transverse diameter, and proved to contain metastases by biopsy, and (e) fixation of axillary lymph nodes to the skin or the deep structures of the axilla.

If these criteria had actually been followed in selecting the patients for operation in our 1915–1934 Presbyterian Hospital series of 640 radical mastectomies, a total of 109 would not have been operated on. Yet the number of patients permanently cured would not have been decreased by a single one.

We have followed this rule for judging operability more or less consistently during recent years at the Presbyterian Hospital, and we have found that it is surprisingly reliable. When we have overstepped these contraindications to operation, as any surgeon is frequently tempted to do, we have not obtained cure in any case.

We have recently completed a review of the 1935 to 1942 (inclusive) cases of cancer of the breast coming to the Presbyterian Hospital. There were 668 primary cases. In 495, or 74.1 per cent, radical mastectomy was carried out. Twenty-five of these patients had inoperable disease ac-

cording to our criteria. Not one of them was cured in five years, and 10, or 40 per cent, developed local recurrence.

Our rule has also been tested by application to the records of the Hartford Hospital[10] and the Barnard Free Skin and Cancer Hospital.[9] In both clinics it has been found to hold true, except for its first category the cases in which carcinoma developed during pregnancy or lactation. Each of these two clinics has 2 patients in this category cured for more than five years by operation. Although the evidence is all too clear that carcinoma of the breast developing during pregnancy or lactation is an especially malignant type, we now are inclined to modify our position and to consider operation in less advanced cases of this type.

### A MORE RADICAL MASTECTOMY

While learning to select our patients more critically for operation, we have tried to extend the scope and to improve the technique of our operative procedure.[5] Following the general plan of the traditional Halsted operation, we remove as much tissue from the chest wall and axilla as we dare, without unreasonable danger to the patient's life or interference with arm function. Our skin incision is planned solely from the viewpoint of adequate removal of the suspected tissues, and so much skin is sacrificed that a skin graft is almost always required to cover the defect remaining on the chest wall. Our skin flaps are cut thinner than in the usual so-called radical mastectomy, and include only the skin itself with its dermal glands and small blood vessels, and the thin layer of fat and areolar tissue lying superficial to the superficial layer of the superficial fascia. Both pectoral muscles, in their entirety, are removed. Traction upon the breast as it is being dissected off of the chest wall is avoided. The axilla is dissected meticulously, usually sacrificing the thoracodorsal vessels and nerve.

With proper attention to the details of technique which insure good wound healing —gentleness in handling tissues, careful hemostasis, and the avoidance of tension in suturing the skin flaps—our technique does not have an added morbidity or mortality, as compared with less radical operations. Edema of the arm rarely develops, and when it does occur, it has not been severe. Indeed, it is less troublesome in our patients than in those of some other surgeons who carry out less radical dissections with a less meticulous technique and obtain poor wound healing. Edema of the arm is due to the fibrosis which follows imperfect wound healing, and is not dependent upon the degree of radicalness of the operation.

### OUR RESULTS

We present our most recent results in cancer of the breast at the Presbyterian Hospital (Table 1). They include the 668 primary cases in the records of the hospital between 1935 and 1942, inclusive. Radical mastectomy was done in 495, that is 74.1 per cent. A score of different surgeons, using varying techniques, performed the operations.

The *absolute* five year survival rate was 47.2 per cent and the absolute five year cure rate 38.6 per cent.

In Table II these results are detailed. The *relative* five year survival rate is seen to be 58.2 per cent and the relative five year cure rate is 48.7 per cent. Local recurrence—including all instances of reappearance of this disease in the operative field in the chest wall and axilla—developed in 14.5 per cent.

Table III shows our results according to the extent of the disease. In 94.9 per cent of the cases treated by radical mastectomy, the disease was operable according to our criteria. In these operable cases the five year cure rate was 71.8 per cent when the axillary nodes were not involved, but it fell to 37.8 per cent when axillary metastases were present.

The results are noteworthy in a group of 25 cases in which the disease was inoperable according to our criteria, yet radical mastectomy was done. Only one of these patients survived as long as five years,

and the local recurrence rate was 40 per cent.

I should also like to present the results (Table IV) in a smaller personal series of cases of cancer of the breast in which my year cure rate was 59 per cent. It is important to point out that in the group of cases in which the disease was limited to the breast 90 per cent were well after five years and none had developed local recur-

TABLE I

Presbyterian Hospital 1935–1942 (inclusive)

| | | |
|---|---|---|
| I. | Total number of female patients with mammary cancer | 787 |
| II. | *Secondary* cases—previous curative treatment elsewhere | 119 |
| III. | *Primary* cases—no previous curative treatment | 668 |
| | Ward—411 Private—257 | |
| | a—No irradiation or surgery | 37 |
| | b—Irradiation only | 107 |
| | c—Irradiation followed by simple mastectomy | 4 |
| | d—Local excision or partial mastectomy | 5 |
| | e—Simple mastectomy | 13 |
| | f—Simple mastectomy plus axillary dissection | 7 |
| | g—Radical mastectomy | 495, or 74.1% |
| | h—Total cases receiving treatment | 631, or 94.5% |

*Absolute Survival and Cure Rates*

In calculating absolute cure and survival rates *no* deductions from the total number of primary cases are made.

| | | |
|---|---|---|
| IV. | *Absolute* 5 year survival rate (315÷668) | 47.2% |
| V. | *Absolute* 5 year clinical cure rate (258÷668) | 38.6% |

TABLE II

Presbyterian Hospital 1935–1942 (inclusive)
Five Year Results with Radical Mastectomy

| | | |
|---|---|---|
| I. | Number of radical mastectomies | 495 |
| II. | Operative deaths | 9, or 1.8% |
| III. | Lost track of before 5 years | 19, or 3.8% |
| | Ward cases—2 Private cases—17 | |
| IV. | Died of unknown cause before 5 years | 7, or 1.4% |
| V. | Died of intercurrent disease before 5 years | 18, or 3.6% |
| VI. | Died of breast cancer before 5 years | 154, or 31.1% |
| VII. | Alive with breast cancer persisting 5 years after operation | 47, or 9.5% |
| VIII. | Alive without breast cancer 5 years after operation | 241, or 48.7% |

*Relative Survival and Cure Rates*

In calculating relative survival and cure rates *no* deductions from the total number of patients operated upon are made.

Patients lost track of, or dying of intercurrent disease before 5 years are counted as dead of breast cancer.

| | |
|---|---|
| Relative 5 year survival rate (288÷495) | 58.2% |
| Relative 5 year clinical cure rate (241÷495) | 48.7% |
| Local recurrence rate (72÷495) | 14.5% |
| 1—on chest wall (69÷495) | 13.9% |
| 2—in axilla (11÷495) | 2.2% |

own technique for radical mastectomy was carried out, usually with a resident surgeon operating and myself assisting him. In this group of 103 operable cases there were no operative deaths, and the relative five rence. This illustrates what can be achieved when a thorough operation is carried out for the so-called Stage I cases. I doubt that irradiation can achieve a higher cure rate, and I know that the morbidity in terms

TABLE III

Presbyterian Hospital 1935–1942 (inclusive)
Five year results with radical mastectomy according to extent of disease

| | |
|---|---|
| A—Cases classed as operable (Haagensen and Stout) | 470, or 94.9% |
| (1) Limited to breast | 189, or 40.2% |
| a—Number of patients surviving 5 years | 144, or 76.6% |
| b—Number of patients cured 5 years | 135, or 71.8% |
| c—Number developing local recurrence | 8, or 4.3% |
| (2) Breast and axilla involved | 281, or 59.8% |
| a—Number of patients surviving 5 years | 143, or 51.1% |
| b—Number of patients cured 5 years | 106, or 37.8% |
| c—Number developing local recurrence | 54, or 19.2% |
| B—Cases classed as inoperable (Haagensen and Stout) | 25, or 5.1% |
| a—Number of patients surviving 5 years | 1, or 4.0% |
| b—Number of patients cured 5 years | 0 |
| c—Number developing local recurrence | 10, or 40.0% |

TABLE IV

Personal Series—Presbyterian Hospital 1935–1942 (inclusive)
Radical Mastectomies—Resident Surgeon Operators

| | | |
|---|---|---|
| A—Cases classed as operable | | 103 |
| (1) Limited to breast | 40, or 38.8% | |
| a—Number of patients surviving 5 years | 37, or 92.5% | |
| b—Number of patients cured 5 years | 36, or 90% | |
| c—Local recurrence | 0 | |
| (2) Breast and axilla involved | 63, or 61.2% | |
| a—Number of patients surviving 5 years | 32, or 50.8% | |
| b—Number of patients cured 5 years | 26, or 41.3% | |
| c—Number developing local recurrence | 12, or 19% | |
| B—Cases classed as inoperable | | 2 |
| Case No. 461444—Brain metastasis mistaken for pituitary adenoma. Died 14 months after operation without local recurrence. | | |
| Case No. 74983—Extensive edema of skin. Local recurrence and pulmonary metastases. Died 14 months. | | |
| Relative 5 year survival rate (69 ÷ 105) | 65.7% | |
| Relative 5 year cure rate (62 ÷ 105) | 59% | |

TABLE V

PRESBYTERIAN HOSPITAL SERIES 1935–1942 (INCLUSIVE). RESULTS OF RADICAL MASTECTOMY ACCORDING TO LENGTH OF OPERATION

| Length of Operation in Minutes | No. of Cases | Operative Deaths | | 5 Year Local Recurrence | | 5 Year Clinical Cure | |
|---|---|---|---|---|---|---|---|
| | | No. | Per Cent | No. | Per Cent | No. | Per Cent |
| I. 1 to 59 min. | 0 | | | | | | |
| II. 60–119 min. | 17 | 1 | 5.9 | 4 | 23.5 | 4 | 23.5 |
| III. 120–179 min. | 74 | 2 | 2.7 | 11 | 14.9 | 33 | 44.6 |
| IV. 180–239 min. | 145 | 2 | 1.4 | 21 | 14.5 | 67 | 46.2 |
| V. 240 or more min. | 259 | 4 | 1.5 | 36 | 13.9 | 137 | 52.9 |

of edema of the arm and limitation of arm function is greater after intensive irradiation than after a satisfactory operation.

Table v presents interesting data which support the advantageousness of a thorough operation. As the length of time devoted to the operation increased in patients operated upon between 1935 and 1942, the cure rate rose and the frequency of local recurrence fell.

A final point to be emphasized regarding our results with cancer of the breast is that they have steadily improved during the last generation. In Table vi the results with radical mastectomy in our hospital are shown grouped in five year periods from 1915 to 1942. It will be seen that the cure rate has doubled since 1915. This improvement appears to have been achieved without the assistance of irradiation, for we have used it but little during recent years. A more critical selection of cases for operation is no doubt the main factor in this improvement in our relative cure rate.

Table VI

PRESBYTERIAN HOSPITAL SERIES—1935–1942 (INCLUSIVE). RESULTS OF RADICAL MASTECTOMY ACCORDING TO FIVE YEAR PERIODS

| | No. of Cases | Operative Deaths | | 5 Year Local Recurrence | | 5 Year Clinical Cure | |
|---|---|---|---|---|---|---|---|
| | | No. | Per Cent | No. | Per Cent | No. | Per Cent |
| I. 1915–1919 | 128 | 3 | 2.3 | 32 | 25.0 | 34 | 26.6 |
| II. 1920–1924 | 127 | 7 | 5.5 | 24 | 18.9 | 37 | 29.1 |
| III. 1925–1929 | 160 | 8 | 5.0 | 42 | 26.3 | 53 | 33.1 |
| IV. 1930–1934 | 225 | 2 | 0.9 | 48 | 21.3 | 107 | 47.6 |
| V. 1935–1939 | 314 | 5 | 1.6 | 52 | 16.6 | 146 | 46.5 |
| VI. 1940–41, 42 | 181 | 4 | 2.2 | 20 | 11.0 | 95 | 52.5 |

### ABSOLUTE CURE RATES

In this symposium we are comparing the results of the treatment of cancer of the breast in several American and foreign clinics. It is at once apparent that a strict comparison of our results is impossible because the cure rates have been compiled in different ways. The unpleasant truth is that almost a half century has gone by since Winter,[11] in a memorable paper published in 1902, outlined the standards for evaluating the results of the treatment of cancer which should be our guide. Except for the League of Nations Committee of European gynecologists and radiologists who in 1928[7] undertook to study the end-results of treatment of cancer of the uterus, very few have followed Winter's method of expressing results in terms of the *absolute*, or over-all cure rates. The absolute five year cure rate is the percentage of the total number of new patients with cancer applying for treatment who are known to be clinically well five years later. The absolute five year survival rate is also a useful figure, and refers, of course, to the percentage of the total number of new patients with cancer who survive five years. Until we all present our results with cancer of the breast in these terms, it will be impossible to decide which method of treatment is the best.

*Relative* five year cure and survival rates, which represent the percentage of patients cured or surviving of the total number treated are of less importance for comparison, because these relative rates are influenced by the selection of patients for treatment. They should, however, be included in all studies of end results.

In compiling our results of treatment of the breast cancers seen at the Presbyterian Hospital between 1915 and 1934, Dr. Stout and I presented absolute as well as relative cure and survival rates, and we have again presented them today for our latest series

of cases, those seen between 1935 and 1942, inclusive.

The League of Nations Committee to which I have referred specified in detail the standards to be used in compiling results of treatment. An important feature of the method recommended is the use of the *total number* of cases in which treatment is undertaken as a basic figure in compiling the results. *No deductions* are permitted for patients failing to complete treatment, or lost to follow-up, or dying of intercurrent disease or unknown cause, within the five year period. All patients in these categories, even if free of clinical evidence of cancer at the time they are lost sight of, or die, must be counted as having died of cancer.

In determining our end results at the Presbyterian Hospital, Dr. Stout and I have followed these standards with care. As will be seen in Table II no deductions from the total number of patients operated upon have been made. In certain other clinics very different methods of compiling end results have been used. Deductions of various groups of cases from the total number treated have been made, thus favorably influencing the cure rate. Adair,[1] in his last comprehensive report of the end results of the treatment of cancer of the breast at the Memorial Hospital (1943) used a method of compiling end results in which he divided his patients into indeterminate and determinate groups. Some 613 patients of a total of 1,996 primary operable cases were placed in the indeterminate group. These 613 cases, which included the patients lost to follow-up, those dying of intercurrent disease before five years, and those in which satisfactory microscopical evidence was not available, were set aside as "not available for exact studies" and were not considered in calculating the cure rate! This concept of an "indeterminate" group of cases seems to us to be basically incorrect. *All* cases are determinate in that they represent the sum total of the curative achievement of the hospital's forces in combatting the disease.

The confusion which results from the use of such widely divergent methods of compiling cure rates is like that which would follow if each one of us calculated his income tax on the basis of an individual method.

In all humility we must realize that our duty to society necessitates the general use of the strictest standards for studying the end results of treatment. The truth is difficult enough to discern even when we discipline ourselves with the most rigorous safeguards against statistical error.

I would appeal for a strict comparison of absolute cure and survival rates, with the hope that with such data we can justly compare the relative merits of different methods of treatment. Only in this way can we hope to find out how best to treat cancer of the breast.*

622 West 168th St.
New York 32, New York

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* For discussion see page 349.

Vol. 62, No. 3

# CANCER OF THE BREAST*

*By* DR. ROBERT McWHIRTER
*Royal Infirmary*
EDINBURGH, SCOTLAND

BEFORE proceeding to give an account of the method of treatment now in use in Edinburgh, perhaps I may be permitted to make some observations which have an important bearing on this discussion.

Cancer of the breast is a common disease and great interest has been taken in its treatment for many years. By using reliable methods of assessment we ought to know by now the true value of each method of treatment and which method will give the best results. The very fact that we do not know is surely a clear indication that our methods of assessment are faulty. Faulty assessments produce great confusion and it is regrettable that it should still be possible to select from the most recent publications evidence which will either support or condemn any method of treatment we care to consider. Each year further contributions are added to this bewildering array, and the competition to produce still higher survival rates continues. That such confusion should exist is a serious matter, for progress is retarded and patients may not always be treated by the method which gives the best results.

We have it in our power to end this state of affairs, and because radiotherapists are so frequently concerned with this problem, I venture to suggest to this meeting that we should take the opportunity at the next International Congress of Radiology to discuss the manner in which results should be presented. If we are successful in this, there is not the slightest doubt that we will render great service not only to ourselves but also to our patients.

More extensive observations have been made elsewhere and time does not permit of their repetition, but briefly it may be said that many authors in presenting their results have failed to appreciate the extent by which selection may distort the value of a method of treatment. Thus, in many publications only the results of cases actually treated are presented and the number of untreated cases may never even be mentioned. Yet it will be agreed that the more carefully patients are selected for treatment the higher will be the survival rates in the treated cases. Even with a poor method of treatment good results in treated cases can always be obtained provided only early cases are selected. These observations are beyond dispute and yet it is this failure to appreciate the influence of selection which causes so much of the present confusion.

It must not be assumed from what has been said that it is wrong to select patients for a method of treatment. Indeed, the reverse is true and we are indebted to Haagensen and Stout for the good service they have done in demonstrating that radical mastectomy when performed in certain types of cases may not only shorten life but may also make the end more miserable. At the same time it is most essential to appreciate that this improved selection, while inevitably providing higher five year survival rates in treated cases, will not save the life of a single additional patient.

It cannot be too strongly emphasized that the true value of a method of treatment depends just as much on the number of cases to which it will apply as on the results obtained when it is applied. Cases considered to be beyond a method of treatment are just as much failures as cases actually treated and failing to be cured. If we wish to avoid the distorting influence of selection we must accept that the only really reliable survival rates are those obtained by expressing the number of survivors as a per-

* Presented in a Panel Discussion on Treatment and Results in Cancer of the Breast at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

centage of the total cases referred. No case must be omitted from this total for any reason whatsoever. Patients who were never admitted to hospital and advanced cases admitted to medical wards for the treatment of pleural effusions, jaundice, cerebral metastases, etc., must still be included in the total on which the survival rate is based.

It is admitted that the proportion of advanced cases will vary from one hospital to another, but it is difficult to see how proper allowance can be made for this. Attempts have been made to overcome this difficulty by means of staging, but of all the methods of staging none are free from variation in interpretation. The same is true of the criteria of operability, for no matter how carefully these are defined, they will always be subject to so much personal variation in interpretation that reliable comparison on the basis of operable cases cannot be made.

Exception, too, must be taken to comparisons by means of "clinical cure rates" or "symptom-free rates." It is necessary to recall that many of these assessments may depend on the statements made by the patient or by the family physician, and that even when the clinical examination is conducted at the clinic it may be extremely difficult to tell whether a patient is free from disease or not. "Clinical cure rates" and "symptom-free rates" cannot be regarded as other than statements of opinion. Survival rates, which are statements of fact, are therefore preferable.

It may also be observed that when the results of treatment are based on all cases coming to a large general hospital, they are of greater value than those obtained in special hospitals and much more reliable than the results of a personal series recorded by individual surgeons.

The adoption of the above basis of assessment will provide results which may come as a great disappointment to those who in the past have been content to calculate the survival rates of only those cases which were fully treated.

Thus while five year survival rates varying (according to the degree of selection) from 35 per cent to 45 per cent may be obtained in cases actually treated by radical mastectomy, I do not believe the five year survival rate will exceed 25 per cent when all cases referred to a large general hospital are included in the total on which the survival rate is based.

Put in another way, the radical operation fails in approximately 75 per cent of cases as judged by the five year survival rate. It was because radical mastectomy was recognized to fail in so many cases that it was decided in Edinburgh to explore the value of other methods of treatment.

The value of combining postoperative radiotherapy with radical mastectomy was first investigated. Table 1 shows the results obtained and it will be noted that the five year survival rate of all cases was 30.9 per cent. The investigation began in 1935 and was continued until 1940.

TABLE I*

DATA FOR YEARS 1935–1940

I. Total number of cases coming to the clinic with breast carcinoma was 932 and of this number 784 were primary cases.

II. Number of primary cases—untreated—130. Of this number 49 had no treatment at all and, in a further 81 patients who had distant metastases when they were first seen, the treatment was directed mainly to the metastases.

III. Number of primary cases—treated—654.

A. The number of cases classified as inoperable was 141.

a. Number of patients surviving at the end of five years = 9—6.4 per cent.

b. Number of patients clinically cured at the end of five years = 6—4.3 per cent.

B. Number of patients classified as operable = 513.

a. Number of patients surviving at the end of five years = 230—44.8 per cent.

b. Number of patients clinically cured at the end of five years = 203—39.5 per cent.

Of the 784 patients with primary tumors 242 were alive at the end of five years—30.9 per cent.

All deaths have been assumed to be due to cancer.

While postoperative radiotherapy was successful in reducing the number of local

* The data in Tables I and II have been presented in accordance with the request made by the American Radium Society.

recurrences, many patients continued to die of distant metastases. This led to the belief that dissection of the axilla might cause dissemination of malignant cells to sites beyond the area which could be irradiated. It will be appreciated that if cells are in fact disseminated then postoperative radiotherapy will fail to save the life of the patient, for no matter how effective it is locally it cannot influence cells outside the irradiated area.

In 1941 the treatment of breast cancer was discussed at a further meeting of the surgical staff and it was decided to continue to remove the breast by surgery but that the treatment of the axilla should be by radiotherapy alone. This decision was made for the following reasons:

1. When the disease is confined to the breast, surgery gives good results. Surgery is thus an effective method of treating the disease in the breast, and it was decided that surgical removal should be continued.

2. While at first sight surgery might appear to be the most satisfactory method of treating the axilla, a more careful examination will show that its value is, in fact, very limited. It is true that the results are excellent when the axillary glands are not involved, but if there are no malignant cells in the axilla it would appear unnecessary to dissect it, for the removal of normal lymph nodes cannot influence the result. On the other hand, when the axilla is secondarily involved, there is universal agreement that radical mastectomy often fails to save the life of the patient. Since, therefore, surgical removal of the lymph nodes is unnecessary when the axilla is not involved and often fails when the axilla is involved, it was decided to treat the axilla by radiotherapy to see if better results could be obtained.

3. In many forms of cancer radiotherapy has now become the treatment of choice, and in breast carcinoma it has been shown that postoperative recurrences can be effectively treated by this means. Immediate postoperative radiotherapy will greatly reduce the number of local recurrences. From these observations it must be concluded that radiotherapy can destroy breast cancer cells and that radiotherapy is at least an alternative method of treating the axilla.

Soon after this method of treatment was introduced it was found that a much higher proportion of patients could be given full treatment than had been possible before. Thus the prospect of cure was offered to a greater number of patients, and, as will be shown later, patients with fixed axillary glands and with glands present in the supraclavicular region were treated with a considerable measure of success.

The wound heals more quickly than after the radical operation. Radiotherapy can, therefore, be applied with less delay, and the interval during which cells may escape to distant sites is thus reduced.

When patients are treated by radical mastectomy and radiotherapy, edema of the arm is common. With simple mastectomy and radiotherapy edema of the arm is almost unknown.

The number of survivors at the end of five years has now been ascertained for the years 1941 and 1942, during which 480 new primary cases were referred. The results are presented in Table II.

TABLE II

DATA FOR YEARS 1941 AND 1942

I. Total number of cases coming to the clinic with breast carcinoma was 521, of which 480 were primary cases.

II. Number of primary cases—untreated = 72. Of this number 21 had no treatment at all and in a further 51 patients who had distant metastases when they were first seen, the treatment was directed mainly to the metastases.

III. Number of primary cases—treated = 408.

- A. Number of cases classified as inoperable = 98.
  - a. Number of patients surviving at the end of five years = 18—18.3 per cent.
  - b. Number of patients clinically cured at the end of five years = 16—16.3 per cent.
- B. Number of cases classified as operable = 310.
  - a. Number of patients surviving at the end of five years = 175—56.5 per cent.
  - b. Number of patients clinically cured at the end of five years = 152—49.0 per cent.

Of the 480 patients with primary tumors, 197 were alive at the end of five years—41 per cent.

All deaths have been assumed to be due to cancer.

Not only is the survival rate high in the operable cases, but it will also be observed that 18.3 per cent of the cases classified as inoperable (according to the standard laid down by Haagensen and Stout) are alive at the end of five years. This remarkably high figure clearly demonstrates that radiotherapy is an effective method of treatment of the axilla even when the axillary involvement is gross.

Attention is drawn to the fact that the number of patients referred each year is much higher than in the period 1935–1940. Since 1941 an attempt has been made to ascertain the incidence of breast cancer in southeast Scotland, and in order to do so the general practitioners in the area have been especially requested to refer all cases to the Royal Infirmary no matter how advanced they are. That most cases are now being referred is indicated in Figure 1.

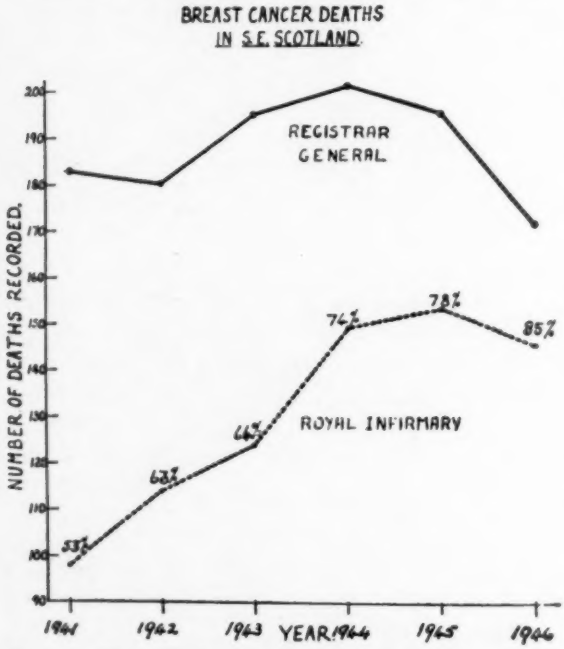


FIG. 1. The number of deaths from cancer of the breast occurring in patients referred to the Royal Infirmary from the southeast of Scotland has been expressed as a percentage of the deaths recorded by the Registrar-General from the same area.

The significant feature in Figure 1 is the fact that nearly all deaths now being recorded by the Registrar-General are occurring in patients already referred to the Royal Infirmary. All or nearly all patients must be referred for several years before such a high percentage is obtained, and it may therefore be assumed that nearly all cases of breast cancer occurring in southeast Scotland are now being referred to the Royal Infirmary. From these observations it can be claimed with considerable confidence that the results obtained during the period 1941–1942 are based on unselected cases. In all probability the results are less influenced by selection than any figures hitherto published. It is almost superfluous to add that if the referral of all advanced cases had not been especially requested, still higher survival rates could have been presented.

A full account cannot be given of all the technical details of treatment by simple mastectomy and radiotherapy and the following is a brief summary of the essential points.

The method of treatment is a combination of two procedures which must be coordinated if the best result is to be obtained.

The following points are of importance in the surgical aspect of treatment.

1. Preoperative preparation by iodine is contraindicated because it lowers the skin tolerance to radiotherapy.

2. The skin incision and the undermining of the skin flaps should be as limited as possible, so that tissue spaces outside the area to be irradiated will not be contaminated with malignant cells liberated during the operation.

3. Excessive skin should not be removed for tension on the skin flaps may be associated with failure of the wound to heal and delay in the application of radiotherapy. Tightly stretched skin flaps do not tolerate irradiation well. Skin grafting does not overcome the difficulty, for grafts do not tolerate roentgen treatment well.

4. Where the primary tumor is mobile on the pectoral fascia, the fascia should not be removed as this promotes fibrosis of the pectoral muscle. If the tumor is firmly fixed to the pectoralis major, the muscle should be removed together with the breast.

5. If there are no palpable axillary glands no dissection should be performed, but superficial mobile glands in the subpectoral region and outside the axillary fascia may be removed. Any further dissection of the axilla will defeat the whole purpose of the treatment method advocated.

6. If the patient is very stout it is better to carry out a radical mastectomy because in stout patients it is difficult to deliver an adequate dose of roentgen radiation to the axilla.

7. Supraclavicular glands should never be removed because these glands are easily and effectively dealt with by radiotherapy.

8. Adhesive should not be applied to the skin after the operation because this lowers the tolerance of the skin to irradiation.

The following points are of importance in postoperative treatment by radiotherapy:

1. Only one full course of roentgen treatment should be given. The practice of repeated courses at intervals of three to six months has no place in the treatment of any form of malignant disease where cure is to be attempted and is just as illogical as partial removal of a tumor at intervals of three to six months.

2. Roentgen treatment should be commenced as soon as possible after the operation; the usual interval is two weeks.

3. Four fields are used and every field is treated every day. The axilla is irradiated by two opposed fields and the anterior field extends up to include the supraclavicular region. The chest wall must be treated by tangential or glancing fields so as to avoid lung fibrosis. The arrangement of the fields is shown in Figure 2.

4. Adequate dosage must be given and in Edinburgh the patients receive a minimal tumor dose of 3,750 roentgens in a period of three weeks. This is the same dosage as is given when clinically obvious local recurrences are treated and it is important not to give less.

5. The roentgen-ray apparatus must be sufficiently powerful to deliver an adequate depth dose in the axilla, and it is doubtful if effective radiotherapy can be given with an apparatus of lower voltage than 250 kv. Heavy filtration is employed and the half-value layer of the beam is 3.7 mm. of copper.

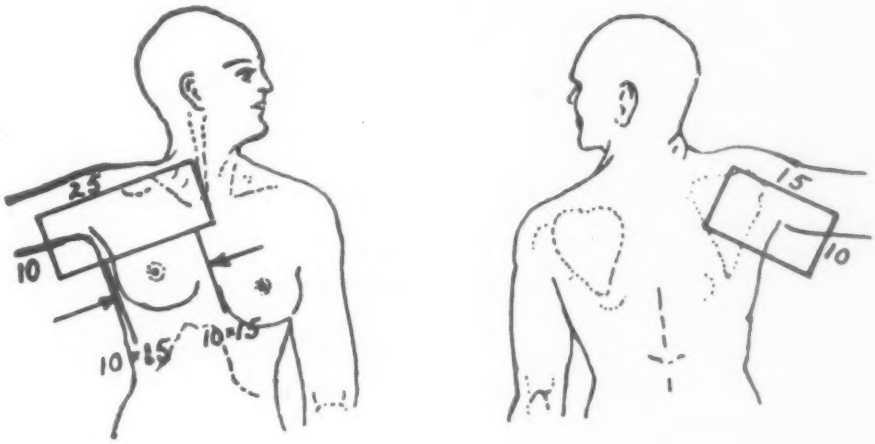


FIG. 2

## SUMMARY

An account has been presented of the method of treatment at present in use in Edinburgh. It must be accepted as representing but one direction in which the survival rates of breast cancer may be improved. There may be other better methods.

Considerable emphasis has been placed on the importance of assessing the true value of a method of treatment so that

better methods may be recognized without undue delay. The view has been expressed that the publication of results of selected cases has greatly confused the issue and has tended to convey the impression that radical mastectomy is a highly successful method of treatment of breast cancer.

When radical mastectomy is the only method of treatment available and when all cases coming to a large general hospital are taken into account, the five year survival rate is unlikely to exceed 25 per cent.

A brief account of the method of treatment by simple mastectomy and radiotherapy has been presented. The five year survival rate of all cases coming to the Royal Infirmary in the period 1941–1942 is 41 per cent.

The most important feature of this method is the substitution of radiotherapy for surgery in the treatment of the axilla. The decision to do so was taken because when the axilla is not involved by malignant cells it appears unnecessary to carry out an axillary dissection and when the axilla is involved the results of surgical dissection are poor.

A high standard of radiotherapy is essential and adequate dosage must be given. It is most important to appreciate that simple mastectomy and a low standard of radiotherapy will be associated with results poorer than those obtained by radical mastectomy without any radiotherapy.*

I would like to express my thanks to my surgical colleagues in Edinburgh without whose support it would have been quite impossible to have carried out the investigation.

Figure 1 has been reproduced by kind permission of the Editor of the *Proceedings of the Royal Society of Medicine.*

Royal Infirmary
Edinburgh, Scotland

* For discussion see page 349.

VOL. 62, NO. 3

# TREATMENT AND RESULTS IN CANCER OF THE BREAST

By GRANTLEY WALDER TAYLOR, M.D.

*Visiting Surgeon, Massachusetts General Hospital and Pondville State Cancer Hospital; Assistant Clinical Professor of Surgery, Harvard Medical School*

BOSTON, MASSACHUSETTS

FOLLOW-UP studies have been carried out on cases of cancer of the breast at the Massachusetts General Hospital for half a century, with special reference to the operable group of cases submitted to radical surgery. During this time, operability has shown no significant change, while the results of operation have improved progressively.

## CURES

In computing cures, all cases submitted to operation are included, except the cases who died of intercurrent disease within the five year period without evidence of recurrent disease; these are omitted as inconclusive. Untraced cases, and patients living with recurrent disease, are recorded as failures. Thus the "cured" cases are those known to be living and free from evident recurrent disease five or more years after operation, plus those dying after five years without evident recurrence.

## OPERABILITY

There is considerable selection exercised by the public and the physicians of the community in the types of cases referred to a general hospital for operation. In recent years, with the establishment of hospitals for terminal care, or for palliative radiation therapy, numerous cases in the later stages are referred directly to these institutions. This practice has the tendency to increase the proportion of operable cases referred to the general hospital. Offsetting this tendency, there has been an increasing discrimination in selection of cases suitable for operation, which has tended to lower the operability rate. In general, the criteria of operability have been followed which were recently formulated by Haagensen and Stout.[9] We drew attention to the unfavorable prognostic significance of many of these factors several years ago.[10] Occasionally, surgical intervention is offered as a palliative procedure in some of the cases not suitable for attempted cure, and these cases have been included in our end-result studies. Thus, in the 1933–1935 series of cases,[8] there were 20 cases in which on the basis of the description in the records the disease had advanced to a stage at which operation with a hope of cure was ill advised. We are not convinced that the progress of the disease is accelerated by these palliative operations; and in many instances the care and comfort of the patient is furthered by them. The operations were performed by a large number of surgeons of the visiting and resident staff, and there is

TABLE I

CANCER OF THE BREAST
Massachusetts General Hospital

| Period | Operability Per Cent | "Cures" Per Cent |
|---|---|---|
| 1894–1904 | 77 | 19 |
| 1911–1914 | 72 | 27 |
| 1918–1920 | 74 | 30 |
| 1921–1923 | 80 | 35 |
| 1924–1926 | 74 | 41 |
| 1927–1929 | 80 | 43 |
| 1930–1932 | 80 | 45 |
| 1933–1935 | 71 | 50 |
| 1936–1940 | 62* | 52 |

* This figure is based upon the total number of breast admissions during this period, including a large number of secondary and recurrent cases.

* Presented in a Panel Discussion on Treatment and Results in Cancer of the Breast at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

some variability in applying the criteria of operability to the individual case. In the series of 395 cases operated upon between 1936 and 1940, there were 3 (0.8 per cent) postoperative deaths.

### RADICAL OPERATION

In general, the operation employed has been a standard radical operation, with removal of the entire breast, both pectoral muscles, and the axillary contents exclusive of the great vessels and nerves. Skin removal is less extensive than that practiced in some clinics, and skin grafting is necessary in less than 10 per cent of the cases. The long thoracic nerve is commonly preserved, and frequently the thoracodorsal nerve and the subscapular vessels. The operation is essentially that described by Halsted and Rodman, and modified by Greenough as described elsewhere.[11] Many of the operations in the earlier series were less radical than those currently employed, and it seems probable that the progressive improvement in results is due to improved surgery as well as to better selection of cases.

TABLE II

CURES IN RELATION TO AXILLARY INVOLVEMENT

| Period | Axilla Free Cures Per Cent | Axilla Involved Cures Per Cent |
|---|---|---|
| 1911–1914 | 56 | 24 |
| 1918–1920 | 54 | 23 |
| 1921–1923 | 62 | 21 |
| 1924–1926 | 64 | 26 |
| 1927–1929 | 74 | 24 |
| 1930–1932 | 70 | 31 |
| 1933–1935 | 75 | 33 |
| 1936–1940 | 78 | 34 |

### FACTORS AFFECTING RESULTS OF OPERATION

*Axillary Metastasis.* The presence or absence of axillary lymph node involvement is the most significant factor in determining the prognosis after operation. At present, it may be said that when the disease is limited to the breast, the chance of cure is about 75 per cent, while when there is axillary involvement, the chance of cure is about 33 per cent. The improvement over the years has taken place in both groups of cases, as shown in Table II.

It should be noted that the pathologists must make a thorough search of the axillary contents and prepare numerous sections of nodes. It is probable that many of the failures among the "axilla free" group already harbor small metastatic foci which might be discovered by more assiduous search. We have also been able to confirm the findings of Warren and Tompkins[12] that the numerical extent of axillary node involvement has considerable significance in prognosis. Thus we found[8] that when only one or two nodes presented metastases, the prognosis was nearly as favorable as in the group without metastases, while the results deteriorated progressively with more extensive involvement. The ratio between cases without axillary node disease to the entire group of operable cases varies some-

TABLE III

GRADE AND PROGNOSIS, 1936–1940 SERIES

| | Axilla Free Per Cent | Cures Per Cent | Axillary Involvement Per Cent | Cures Per Cent | Local Recurrence Per Cent |
|---|---|---|---|---|---|
| Grade 1 | 100 | 100 | 0 | 0 | 0 |
| Grade 2 | 52 | 80 | 48 | 47 | 7 |
| Grade 3 | 30 | 72 | 70 | 26 | 13 |

what, but in general ranges from 30 to 40 per cent. It was 41 per cent in the 1936–1940 series.

*Grade of Malignancy*. Several years ago Greenough[13] applied to mammary cancer the method of grading malignancy developed by Broders for squamous carcinomas. We have found the grade of malignancy to be of very great significance in the prognosis of breast tumors. There is a correlation between the grade of malignancy and the presence of axillary metastasis. Even when cases of comparable extent are considered, it is evident that the high grade malignancy cases present a poorer prognosis.

Table IV

SUMMARY—CANCER OF THE BREAST
Massachusetts General Hospital

| Years | 1894 to 1904 | 1911 to 1914 | 1918 to 1920 | 1921 to 1923 | 1924 to 1926 | 1927 to 1929 | 1930 to 1932 | 1933 to 1935 | 1936 to 1940 |
|---|---|---|---|---|---|---|---|---|---|
| Total primary cases | 468 | 103 | 134 | 183 | 208 | 220 | 231 | 328 | |
| Radical operations | 360 | 74 | 100 | 148 | 158 | 180 | 185 | 236 | 395 |
| Operability per cent | 77 | 72 | 75 | 80 | 74 | 80 | 80 | 72 | |
| Died without recurrence in less than 5 years | | | | 6 | 11 | 10 | 11 | 14 | 11 |
| Axilla free per cent | 33 | 31 | 30 | 28 | 41 | 36 | 37 | 40 | 41 |
| Cures per cent 1 A cases | | 56 | 54 | 62 | 64 | 74 | 70 | 75 | 78 |
| Cures per cent 1 C cases | | 24 | 23 | 21 | 26 | 24 | 31 | 33 | 34 |
| Cures per cent All Ops. | 19 | 27 | 30 | 35 | 41 | 43 | 45 | 50 | 52 |

*Other Factors*. There are numerous other characteristics which appear to have a distinct bearing on the prognosis following operation. In a previous study[14] it was shown that the *age* of the patient was significant chiefly in that young women have a greater proportion of carcinomas of high grade of malignancy, and that axillary lymph node involvement may occur earlier in the course of the disease. The *duration* of the primary tumor is of great significance in the individual case; in that the earlier the operation is performed, the less likelihood there is of metastasis having occurred. The *size* of the primary tumor is related to its duration, grade of malignancy, and perhaps the age of the patient; and we have shown that small tumors have a much more favorable prognosis than large tumors.[8,10] *Skin involvement and ulceration* present a poor prognosis as noted among the contraindications to operation.[9,10]

## RADIATION THERAPY

Radiation therapy has been used in the treatment of inoperable and of recurrent lesions, and in occasional small groups of cases as preoperative or postoperative prophylactic therapy. The details of radiation dosage and technique have varied over the years. At present prophylactic postoperative irradiation is employed only in cases in which the surgeon believes that he has left gross disease. We have been unable to establish that prophylactic irradiation has improved the results of operation, or has decreased or deferred the appearance of operative field recurrences.

## HORMONE THERAPY

In recent years significant aids in the treatment of breast cancer have developed in the revived employment of castration, and in the use of estrogenic and androgenic hormones. Castration may be effected by means of irradiation or by operation. At present, we employ surgical in preference to irradiation castration, on the ground that the results are more dependable and more promptly achieved. In a series of cases

treated several years ago by prophylactic irradiation castration following radical mastectomy,[15] we found no increased curability in this group as compared with a control series. Accordingly, we now do not employ castration prophylactically, but only in the treatment of inoperable and recurrent cases in young women. The most striking favorable results are observed in patients with skeletal metastases. Estrogenic hormones are employed in the treatment of inoperable and recurrent carcinoma, especially in elderly patients in whom benefit is shown chiefly in regressions of local and lymph node disease, and of pulmonary metastases. Androgenic hormones appear to be beneficial primarily in patients with skeletal metastases. These adjuvants are too recent to warrant conclusions as to their place in the treatment of mammary carcinoma; and at present their employment is experimental.

## CONCLUSION

In our opinion, the treatment of operable cancer of the breast is by radical surgery, which may be expected to effect a five year "cure" in about 50 per cent of patients submitted to operation. When there is no axillary involvement, about 75 per cent are cured, while when there is axillary involvement the cures are about 33 per cent. Narrowing of the criteria of operability will result in lower operability and at the same time increase the percentage of cures among the cases submitted to operation. In our experience, the employment of prophylactic irradiation, preoperatively or postoperatively, does not increase the number of cures nor defer recurrences.*

264 Beacon St.
Boston 16, Mass.

* For discussion see page 349.

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# CANCER OF THE BREAST*

By DR. BRIAN W. WINDEYER

*Professor of Radiotherapy, University of London; Director of Meyerstein Institute of Radiotherapy, Middlesex Hospital, London*

LONDON, ENGLAND

THE material on which my contribution to this discussion is based consists of 1,091 patients suffering from cancer of the breast who sought advice and treatment at the Middlesex Hospital during the years 1936–1942. These years have been chosen because they follow the period 1926–1935 which was the basis of the recent survey by B. M. Truscott of cases of cancer of the breast treated at this hospital, and they include all cases up to 1942 which is the last year on which full five year statistics can be based. In 1936 also the roentgen therapy and radium departments were merged into the present radiotherapy department and there was a radical alteration in the technique of roentgen therapy in the treatment of cancer of the breast.

The total number of 1,091 patients who applied for treatment is made up of the following groups:

(a) 977 patients who had had no previous treatment.

(b) 114 patients who had been submitted to operation at other hospitals by a variety of surgeons with some variation in the type of operation performed and who had been referred for postoperative roentgen therapy.

Of the first group of 977 patients, 60 received no treatment—44 because they were considered to be too advanced and 16 because they refused the treatment offered—917 were treated by surgery, or radiotherapy, or by a combination of these methods.

This group of 917 cases was divided into stages according to the clinical classification adopted at Manchester which is as follows:

*Stage I.* The growth is confined to the breast. Involvement of the skin directly over and in continuity with the tumor does not affect staging provided that the area involved is small in relation to the size of the breast.

*Stage II.* As Stage I but there are palpable mobile lymph nodes in the axilla.

*Stage III.* The growth is extending beyond the corpus mammae as shown by:

(a) The skin is invaded or fixed over an area large in relation to the size of the breast.

(b) The tumor is fixed to underlying muscle. Axillary glands may or may not be palpable but if glands are present they must be mobile.

*Stage IV.* The growth has spread beyond the breast area as shown by:

(a) Fixation of axillary nodes indicating extension outside the capsule.

(b) The tumor is completely fixed to the chest wall.

(c) Secondary lymph nodes in supraclavicular region.

(d) Secondary deposits in skin wide of tumor.

(e) Secondary deposits in the opposite breast.

(f) Distant metastases, e.g. bone, liver, lung, etc. The results of treatment have been summarized in Table I.

The methods of treatment which have produced these results have shown considerable variation throughout the series as they have been adapted to the treatment of individual cases in different stages of the disease, and because the series of cases is a composite one, representing the work of a number of surgeons and of the radiotherapy department. In general radical mastectomy was used in Stage I cases, radical mastectomy with postoperative roentgen therapy was used in Stage II and the majority of

* Presented in a Panel Discussion on Treatment and Results in Cancer of the Breast at the Thirtieth Annual Meeting of the American Radium Society, Chicago, Ill., June 20–22, 1948.

Stage III cases; roentgen or radium therapy alone or in some cases associated with conservative surgical excision was used in the remainder of Stage III and in Stage IV cases.

The most obvious fact which appears from Table I is that in comparison with other published work the results in Stage I show a relatively low five year survival and the results in Stages II and III show a relatively high five year survival. This is obviously accounted for by the fact that the classification adopted is a clinical one which seemed most appropriate for this composite series. It is generally recognized that a clinical classification of Stage I will include an appreciable percentage of cases with glands found on histopathological examination to be involved with cancer, and that the percentage of five year survivals will be lower than when Stage I is based entirely on a histopathological classification. Similarly a clinical classification of Stage II will inevitably include some cases in which the enlarged glands are found to be uninvolved on histopathological examination and the results in terms of five year survival will be better than when Stage II is based entirely on a histopathological classification.

The results have been described in terms of five year survival as it has been impossible, in restarting our follow up department after the war, to ensure the attendance of every patient for examination to determine their freedom from disease and some information had to be obtained by correspondence. The follow up has been successful to the extent that only 24 of the 917 patients remain untraced, i.e., 2.6 per cent. For the years 1936–1937 on which the ten year figures are based the untraced are 2 of the 282 patients, i.e., 0.7 per cent. No deductions have been made for the untraced patients and the results are a crude survival rate of all patients treated.

A comparison of the results of radical mastectomy alone, with those of radical mastectomy in combination with radiotherapy in various stages was considered, but it was obvious that any such compari-

TABLE I

CANCER OF THE BREAST

| | 1936–1942 | | 1936–1937 | |
|---|---|---|---|---|
| | Cases treated | 5 year survivals | Cases treated | 10 year survivals |
| Stage I | 255 | 160 = 62.7% | 71 | 30 = 42% |
| Stage II | 193 | 67 = 34.7% | 51 | 16 = 31% |
| Stage III | 235 | 66 = 28% | 84 | 14 = 16.6% |
| Stage IV | 234 | 19 = 8% | 76 | 2 = 2.6% |
| | 917 | 312 = 34% | 282 | 62 = 21.9% |

| | | 5 year survivals | 10 year survivals |
|---|---|---|---|
| 1925–1935 (Truscott) | Treated cases | 24.8% | 10.9% |
| 1936–1942 | Treated cases | 34% | 21.9% |

| | | | |
|---|---|---|---|
| Haagensen and Stout | Absolute 5 year survival | 25.3% | All cases referred |
| Middlesex Hospital 1936–1942 | | 31.9% | All cases primary cancer referred |
| McWhirter 1935–1940 | | 32.4% | All cases referred |

son in this series could not be of value as the groups of cases were not unselected. With some exceptions it was the general rule that cases which appeared to have a worse prognosis at or after operation would be referred for postoperative radiotherapy, and a true comparison of the relative merits of the two methods of treatment could not be obtained. For such a comparison to be of value in a series such as this it would be necessary to plan beforehand and to treat groups by both methods in which the selection was a purely random one.

This series of cases may, however, be of some value for comparison with the over-all results of treatment of the survey made by Truscott of the cases treated in the previous ten years and also for comparison with other published results. It is particularly of value for comparison with Truscott's series as they both represent the total number of cases coming to the same hospital and there is unlikely to be a great difference in the quality of the material, although the present series is from the following decade.

Truscott found that an analysis of 836 treated cases of primary cancer of the breast gave 24.8 per cent of five year survivals and 10.9 per cent of ten year survivals. The figures of this series show 34 per cent of five year survivals of treated cases and 21.9 per cent of ten year survivals of treated cases, an increase of 10 per cent at both five and ten years.

Haagensen and Stout found an absolute five year survival of 25.3 per cent from a total of 1,040 cases referred to the hospital. In the present series there are 312 five year survivals from a total of 977 cases of primary breast cancer referred to the hospital, i.e., a survival rate of 31.9 per cent. The ten year survival rate from 300 cases of primary breast carcinoma referred to the hospital is 62, i.e., 20.6 per cent. The absolute five year survival rate in the present series is 365 from a total of 1,091 which is 33.4 per cent but this is not truly comparable with Haagensen and Stout's figure as it is improved by the inclusion of 114 cases referred for postoperative radiotherapy after operation elsewhere. Of these there were 49 five year survivals, or 42.9 per cent.

The figures for five year survivals in the present series are very similar to those quoted by McWhirter for the period 1935–1940 when the main method of treatment at Edinburgh was radical surgery and postoperative radiotherapy. In his cases there were 32.4 per cent of five year survivals from a total of 790 patients treated.

The most obvious change in treatment which may account for the marked improvement in results compared with those described by Truscott was the alteration in radiotherapy technique which took place in 1936. From that time postoperative radiotherapy has been given as an intensive course of roentgen therapy, using 220 kilovolts, with a half-value layer of 2.1 mm. of copper. The whole of the chest wall on the operated side has been treated by two opposing tangential fields, irradiating from the opposite side of the sternum to the posterior axillary line. The axilla, retroclavicular and supraclavicular regions have been treated by two opposing and posterior fields. The total dose given has been routinely 2,500 to 3,500 roentgens, delivered over a period of thirty to thirty-five days. This treatment came to be used more extensively following radical mastectomy in the cases with axillary metastatic involvement. There was also a tendency to restrict surgical intervention in the more advanced cases and to rely on radiotherapy in the form of roentgen treatment or radium implantation, or a combination of both.

The cases described by Haagensen and Stout were a similar unselected series to those forming the material for this paper as they represented the total cases seen at a large general hospital. The main method of treatment used was radical mastectomy although preoperative and postoperative irradiation had been used in some cases. The authors have concluded that there is no evidence that the additional radiotherapy has had any influence in improving the results of radical mastectomy. In their cases, however, as in the present series, it

was not possible to obtain a true comparison of the results of radical mastectomy alone with those of radical mastectomy and postoperative radiotherapy as the groups were not unselected; and from the evidence produced it seems that this question remained unsolved. It seems, however, that the technique of roentgen therapy employed throughout their series of cases, which were treated prior to 1934, was less intensive than that described in this present series. It may be argued that the improvement in results which has been shown in the cases which I have reported is related to the more intensive roentgen therapy. The similarity of these results from the Middlesex Hospital with those from Edinburgh during the period 1935–1940, when radical mastectomy and postoperative radiotherapy with very similar technique was the main method employed, tends also to confirm this view.

It may be of value to consider the so-called "operable" groups of cases. With the adoption of the criteria of inoperability of Haagensen and Stout the cases in Stage IV and some of the cases in Stage III in this series will be considered inoperable. A consideration of Stages I, II and III as "operable" will therefore give a high operability rate with a somewhat low five year survival rate (Table II).

Consideration of the group of 114 patients who had been submitted to operation elsewhere and referred for postoperative roentgen therapy showed that there were 49 five year survivals, i.e., 42.9 per cent. This group also is likely to give a lower five year survival rate than that of all "operable" cases as it is to some extent selected because the earliest cases with no axillary metastases were rarely sent for postoperative roentgen therapy.

The analysis of this series of cases may have contributed something towards producing a yardstick of what can be achieved by radical mastectomy in early cases, radical mastectomy and postoperative roentgen therapy in later operable cases, and radiotherapy in advanced cases. These are the results of treatment up to the last year on which five year results could be produced. Since that time there have been many cases under treatment and there has been some evolution in technique.

I do not now propose that treatment planned on the basis described is the best than can be obtained. The use of preoperative roentgen therapy has some advantages over postoperative treatment. There are many difficulties in delivering an adequate dose of roentgen radiation to the chest wall as a postoperative measure following radical mastectomy. There is little tissue covering the ribs and the blood supply of the area has been seriously disor-

TABLE II

OPERABLE CASES

| | 1936–1942 | | 1936–1937 | |
|---|---|---|---|---|
| | Cases treated | 5 year survivals | Cases treated | 10 year survivals |
| Stage I | 255 | 160 | 71 | 30 |
| Stage II | 193 | 67 | 51 | 16 |
| Stage III | 235 | 66 | 84 | 14 |
| Total operable | 683 | 293 = 42.9% | 206 | 60 = 29% |
| Operation elsewhere; postoperative roentgen therapy | 114 | 49 = 42.9% | | |

dered. There is the risk of necrosis of skin and also of underlying ribs. From my experience of the irradiation of border line and advanced cases and more recently of operable cases, I am sure that preoperative irradiation can be given with more adequate dosage, with less risk, and without impeding the healing of a subsequent radical operation. It will be necessary to wait some time to see the results of our cases in terms of five year survivals, but I am convinced that there is sufficient evidence available to advocate, (1) for *all* inoperable cases radiotherapy alone with possible subsequent local removal or excision; (2) for *all* operable cases preoperative roentgen therapy followed by radical mastectomy. There are obviously many early cases with no axillary metastases and in these I do not think that associated roentgen therapy is likely to improve the survival figures. It is, however, impossible on clinical examination to eliminate patients with histopathological involvement of glands which are not clinically palpable. Therefore in order to obtain the maximum survival figure the routine use of preoperative roentgen therapy in *all* operable cases would seem to be a rational procedure.

Meyerstein Institute of Radiotherapy
Middlesex Hospital
London, England

## DISCUSSION OF PANEL DISCUSSION ON TREATMENT AND RESULTS IN CANCER OF THE BREAST*

Dr. Maurice Lenz (Moderator of the Panel Discussion), New York. This most interesting panel discussion on "The Treatment and Results in Cancer of the Breast" illustrates the divergent views which the discussants held on the relative merits of radical versus simple mastectomy, and mastectomy with and without preoperative and postoperative roentgen therapy. Of all the speakers only Professor McWhirter has championed simple mastectomy and treatment of the axilla solely by roentgen radiation. He used a tumor dose of 3,750 roentgens in three weeks. It may be questioned whether this dosage suffices to destroy every cancer cell in the axilla, or whether radical mastectomy, including axillary dissection, should remain the treatment of choice. He is probably right, however, in his preference for two instead of multiple opposing fields and in the use of scattering material to make the distribution of the radiation in the depth more homogeneous. He may also be correct in that part of the tangential beam directed at the breast laterally and mesially may be absorbed by the ribs. In our arrangement of the fields crossfiring the tumor, however, this loss, we believe, is insignificant.

Our hesitance to accept 3,750 r in three weeks as adequate to destroy mammary cancer is based on information obtained from a study of three series of patients who received roentgen therapy for cancer of the breast at the Presbyterian Hospital, New York, from 1923 to 1940. The first was a series of 78 patients receiving tumor doses of 300 to 2,300 r in a few weeks after mastectomy. Five year survival in this group of patients was about the same as in patients who were not irradiated after radical mastectomy, and skin recurrences in 8 of 9 instances developed in the irradiated area. The second series consisted of 38 patients who were given tumor doses of 4,500 r in two months, and had radical mastectomy a few days to one year after the roentgen therapy. The tumor dose was calculated at the center of the palpable tumor, in the breast and axilla. Many tumors disappeared grossly, and on microscopic examination there were noted marked retrogressive radiation changes in the cancer cells. In all of the specimens, however, some recognizable cancer cells were still present and complete destruction of the cancer could not be claimed in a single instance. The third series consisted of 32 nonoperated patients receiving tumor doses of 6,000 to 8,000 r in three to three and a half months. Of the 32 patients, 10 with disease limited to the breast and axilla are now free from clinical evidence of mammary cancer eight to ten years after treatment. Viable cancer cells may still lie dormant in the depth of the irradiated breast and axilla, but clinically there is no evidence of growth. There were not any five year survivors among patients with skin metastases en cuirasse or other evidence of extension beyond the breast and axilla, or when the tumor dose was less than 5,500 r. Baclesse reported clinical disappearance "in a significant proportion, only after a dose of about 5,000 r." Our own experience just quoted suggests that long

* Papers by Drs. Baclesse, Berven, Cade, Haagensen, McWhirter, Taylor, and Windeyer.

term clinical arrest of cancer of the breast is more likely after higher dosage. Therefore, we do not believe that the much weaker dosage used in routine postoperative roentgen therapy ever destroys mammary cancer completely. We reserve this weaker treatment for cases in which the surgeon, or preferably the microscopist, believes that the cancer has not been completely removed and give it in the hope of producing temporary growth restraint. The addition of preoperative and postoperative roentgen therapy in cases of borderline operability seems less efficient than stricter separation of cases into those suitable for radical mastectomy and those which should not be operated on. The former need not be irradiated and the latter should be treated only by radiotherapy. We prefer to follow this policy although we respect Berven's leaning toward preoperative roentgen therapy as well as Cade's and Windeyer's reliance on postoperative treatment. Taylor of the Massachusetts General Hospital and Haagensen of the Presbyterian Hospital have shown that strict selection of cases for mastectomy and increased operative experience result in improvement of surgical statistics. If selection of patients with mammary cancer for operative treatment would be more severe, there would be less need for preoperative and postoperative roentgen therapy.

DR. FRANK E. ADAIR, New York. This is a remarkable symposium. The results of therapy of breast cancer are presented from five countries and seven different clinics. The interesting fact in comparing these papers is not their great differences but in the striking similarity of therapeutic results. These can be best brought out by Table 1 which I have built from the submitted abstracts of the authors. Unquestionably, the cancer material differs as well as the irradiation and surgical skills in different clinics. But probably the greatest cause of differences in results is the varying methods of handling the *statistics*, which does differ greatly in each clinic. There is a crying need for uniformity in this field. Until all use the same *statistical* technique, results will be only mildly comparable.

There is a tendency on the part of some authors to a high degree of selectivity of material. This is not proper procedure unless the total material is reported. One must give not only the report on the material operated on, but it is equally important for us to know what happened to the material which was turned down; and was not operated on. One of the most common and inexcusable faults in the study of cancer cases is the selection of only good cases on which to operate. As Taylor brought out, Grade 1 breast cancer is capable of cure in 100 per cent. If one were interested only in a high cure rate, obviously he would select Grade 1 material. The same holds for other cases such as cases of pregnancy with breast cancer. I think it is wrong to classify such cases as inoperable and deny them their chance of cure even though it is not favorable material. However, in the light of Barney Brooks' study on his cases of pregnancy, in which he obtained 38 per cent survival at the end of five years, and of my own material in which 25 per cent were alive at the end of five years, I feel that it is improper to classify the *breast cancer-pregnancy* cases as inoperable. Similarly, many other manifestations of breast cancer which are unfavorable (but not constituting inoperability) should not be excluded just in order to attain a high cure rate in a small, highly selected group. As yet, radiation therapy and hormones are not to be relied on for cure of breast cancer. A glance at Table 1 shows those operable cases treated by irradiation alone in the hands of Baclesse and Adair gave only 21 and 25 per cent respectively. With such accomplishments, one should consider seriously our personal responsibility before denying a patient a radical operation, when the next best agent we have at present possesses only half as many cures.

Berven reports a very low rate (3 per cent) of local recurrence. Cade reports the highest cure rate of all, namely 87 per cent in those cases of disease confined to the breast. They were treated by surgery alone. His studies are especially interesting as they give the comparative figures of cases treated by radium alone, and surgery plus radium. Haagensen's local recurrence rate is interesting (11.4 per cent) as he constantly emphasizes the routine skin graft in his writings. Today, with patients coming so much earlier for therapy, before the tumors become bulky, I do not think a routine skin graft necessary. It should be here brought out that a helpful addition to breast surgery is the greater use of loosening up the skin over the sternum and making greater employment of the opposite breast for repair of the plastic defect. McWhirter has presented a stimulating and controversial paper. His clinic is unique in that practically all the breast cancer material in that portion of Scotland filters into his radiation clinic.

TABLE I

"OPERABLE" BREAST CANCER

| | Baclesse | Berven | Cade | Haagensen | McWhirter | Taylor | Windeyer | Adair |
|---|---|---|---|---|---|---|---|---|
| Five year cures; Stages I and II combined | | | | 48% Presbyterian Hospital; 59% Personal series | Radical +roentgen irradiation =39.5%; Simple +roentgen irradiation =48.7% | 50% | | 59.2% |
| (Stage I) Breast alone involved | | 60 to 61% | Radium=70% Surg+Ra=78% Surgery=87% | 71% | Radical 80% | 75% | 62.7% | 83.2% |
| (Stage II) Breast and axilla involved | | 30 to 34% | Radium=25% Surg+Ra=35% Surgery=29% | 37% | Radical 45.4% | 33% | 34.7% | 44.3% |
| Per cent having axillary involvement | | 62.3% | | 62% | | 60% | | 62% |
| Local recurrence | | 3% | | 11.4% | | 7 to 10% | | 10% |
| Operative mortality | | | 1.65% | 1.8% | | 2% | | 0.29% (1 in 325) |
| Five year cures by irradiation alone | 21% | | | | | | | 25% |

To me, his paper would indicate that the best way *not* to treat operable breast cancer is by a simple mastectomy with subsequent radiation therapy. His radical mastectomy material gives 80 per cent survival in those cases having disease confined to the breast; which is extremely gratifying. Curiously, in his over-all cure rate of operable material, the radical plus roentgen treatment gave 39.5 per cent; while the simple mastectomy plus roentgen therapy gave 48.7 per cent. This is contrary to our experience at Memorial Hospital, where we have been disappointed in the results of irradiation in axillary disease, due to the great spottiness and irregularity of results accomplished by irradiation there.

Taylor's results represent a high standard of competency. His definite statement that postoperative irradiation produces more cases of lymphedema of the arm is arresting. It signifies that we must balance the good accomplished by irradiation against the evil which it produces by adding to the number of lymphedema cases.

Professor Windeyer's contribution as usual is sound and brought out many valuable points.

The Radium Society is to be congratulated on the high quality of this Symposium.

DR. BERVEN (closing). Dr. Adair's table needs correction as our table pertains to cure rate and not survival. For Stage II it is 24 per cent for the period 1921 to 1935, and 40 per cent for the later period.

Someone asked "Since five year results may vary as much as 20 per cent or more from one to another of two hospitals in your own city, would it not be better to judge the usefulness of adjunct radiotherapy on the basis of its ability or inability to reduce local recurrence below a minimum?" Only one of the two hospitals is in our city. The other material comes from county hospitals all over Sweden. Our local recurrences are very low. They are only 3 per cent.

If you use the same method of treatment in a

different material you get different results. In Karolinska Hospital we have all patients, early cases in Stage I, more advanced cases in Stage I, all cases in Stage II, and we see the difference in results; 80 per cent in Stage I and 45 per cent in Stage II. The material coming from the county hospitals is different. The surgeons in the county hospitals do not send the very early cases in Stage I or II to the Radiumhemmet but send the bad inoperable cases with periglandular extension which they have tried to operate on. This accounts for the fact that in spite of the same method of treatment, the results are different, depending upon the clinic from which they came.

SIR STANFORD CADE (closing). I should like to answer a question about the method of irradiation which I believe was asked by the Chairman. Up to the period of 1938, and that is why I put radium and surgery in my tables, irradiation of breast cancer was carried out by radium; that is, interstitial radium needles plus a surface applicator. By this method we can raise the tissue dosage to very high figures, 9,000 r. In a small group of cases, perhaps 20 or 30, but no more, teleradium alone was used. Since 1938 we have reversed our irradiation of the breast to comprise what we find is a more flexible and an equally effective method.

DR. HAAGENSEN (closing). I did make a plea for absolute cure rates and I presented such figures.* They were 38.7. The absolute survival rate, if we might distinguish here between survival and cure, was 47.3. These are absolute cure rates and survival rates, and if all of us had these figures from all the larger cities of the world, we would perhaps be able to show that in clinics where there is a greater tendency toward radical surgery, the results are worse perhaps or better than in those clinics where there is a greater tendency toward the use of radiation. This would be a crude sort of differentiation which we might use to advantage.

Someone asked how many patients who do not have involved lymph nodes clinically, that is Stage I, actually have them microscopically. In our experience 45 per cent of the patients in whom no lymph nodes were palpable proved to have axillary metastasis. This is a very great and to us an inseparable objection to the matter of basing your plan of treatment on whether or not the patient on clinical grounds has axillary nodes. We feel that we must give every patient the treatment which we think is best for patients that have axillary involvement and that means the most radical surgical attack.

I am sure that at least six months' time would be lost in the surgical attack if we gave adequate preoperative roentgen therapy, say, a tumor dose of 5,000 or 6,000 r, and there would also be real surgical hazards involved in doing the kind of radical mastectomy we try to do after that much radiation. Either we rely on surgery, the best kind of surgery we can do, or we do not use surgery and rely on irradiation.

Surgery has not yet exhausted all its possibilities. We can still attack the mediastinum, which is the second most important route by which the disease extends. This is a logical surgical attack and we have begun to do it in a small way.

DR. MCWHIRTER (closing). Let me repeat right at the beginning that this investigation which has been done in Edinburgh is still in an incomplete stage. I agree completely that the information will be much more reliable after ten years. It will become, indeed, very reliable if the Registrar General does not let us down.

I was impressed by the slides shown by Dr. Baclesse in cases treated by radiotherapy alone, and I was impressed, too, with the cases shown by Dr. Lenz treated by radiotherapy alone after a period of ten years. I, too, have cases treated by radiotherapy alone after ten years, because while one intends to treat the majority of the patients by simple mastectomy and radiotherapy, obviously in many of the advanced cases it is not possible to do any operation at all, nor is it advisable.

In the cases such as Sir Stanford Cade showed with gross involvement of the breast, even simple mastectomy would be an entirely wrong procedure. These cases we treat by roentgen irradiation alone.

"If survival rates are based on vital statistics are they not subject to errors of clinical judgment unless all causes of death are established by postmortem examination?" was asked me, and also "What is your proportion of local recurrences?"

As to this statistical difficulty, which we are so constantly up against and which led me to make the plea that at the next International Congress we consider very seriously a common language of figures, Professor Berven showed

* Dr. Haagensen made slight changes in some of the figures given in his paper when proof was sent to him.—ED.

the difference in two hospitals and he has explained that, but if he worked at one hospital and someone else worked at the other the results would be different, different because the material is basically different. That I think is the very important point which comes out there. Perhaps I should put my figure on the blackboard. I take Paterson's classification of Stages I and II as being the truly operable cases. On that basis this is radical surgery plus roentgen irradiation. Histopathologically negative glands at the end of five year survival rate, 80.5 per cent and with glands histopathologically positive, 45.4 per cent.

I cannot give the figures for simple mastectomy, obviously.

I was very impressed with Dr. Haagensen's figures. They are extraordinarily good, but I think there is a difference in the material which we compare. In the personal series, which he indicated, only 2 out of 103 were inoperable. I presented 15 per cent inoperables due to the fact that we collect large numbers of advanced cases from hospitals where patients are admitted often with other conditions or in terminal stages of breast cancer.

Again I return to the question of selection, and in Dr. Taylor's figures the best results were in the most recent years where the selection was highest. Even when the glands were not involved the figure progressively increased over the years. I find difficulty in understanding why that should be unless it has been on the basis of selection. There was also a progressive improvement in the cases where the nodes were histopathologically involved. That is understandable because there has been a general tendency for the operation to become more radical and for the cases to be more carefully selected so far as skin involvement is concerned.

May I just make a further point. In my cases presented there were approximately 40 different surgeons operating. Some of those men are attached to small hospitals. If I take one surgeon's figures who is particularly interested in breast cancer and has tried out a large number of operations, his figures are 10 to 15 per cent higher than I have shown you. A personal series would always be higher than a general hospital figure, and considerably higher if one attempts to take in all the cases in the area served by the hospital.

I should like just to impress, too, that not all the cases were treated by simple mastectomy and radiotherapy, only cases where that appeared to be indicated. In a large number of cases that was impossible.

I apologize for the misunderstanding about propaganda to the public. That has been my policy in southeast Scotland and it does not extend beyond that. Because of the rate of error in diagnosis I do not believe that the medical profession yet has accepted the viewpoint that any lump in the breast is a cancer until proved otherwise.

How do we know that we produce sterilization in the area? Well, we don't, but the patients are alive. They are symptom free. They are useful members of society. They have no complaints. I say this quite deliberately. They may still have cancer cells present. From the discussion I still think the method, so far as it goes, has proved quite sound. It is perhaps better to have a patient alive with a few cells which are not causing any trouble than dead.

The question of the use of vital statistics. I agree that the death certification is quite unreliable in many sites. One could not use this method, for example, in the evaluation of cancer of the stomach. It would be quite unreliable, but I will put this point to you. It must seldom happen that a patient is certified as having died from breast cancer unless in fact she had breast cancer. I think that point comes out clearly, and it may be that a number of patients who had a breast removed and who died from some other causes were certified as having died from breast cancer, but you see that loads against the argument which I presented to you. As to the percentage of local recurrences, I cannot give that figure directly. All I can say is that it is extremely low.

Dr. Lenz posed the question that 4,500 r will not sterilize the breast area. That I think is in two months' time. The dosage which we give, 3,750 r in three weeks, is probably a higher biological dose. There are three other points which I would make there. Dr. Lenz uses multiple fields. I am perhaps wrong but I believe firmly that if one is to obtain reliable statements of dosage there should be two opposed fields only, and that if there are multiple fields one can arrive at erroneous conclusions as to the minimum dose in the tumor area. One may calculate the obvious dose or a dose at a particular point, but the dose should be calculated at every point in the possible area of involvement. There is a tendency, too, and I am not sure whether that operates in Dr. Lenz's cases, to direct a field straight into the axilla. That I

think is wrong because the axillary skin will not tolerate dosages well, and while the skin reaction may be very marked, the rapid falling off in dosage in the axilla will not produce good results.

The question of bolus scattering material in the area again I think is extremely important. I am surprised to find that frequently bolus material is not used. If two opposed fields are used with the breast in situ and no bolus is added, the dosage on the summit of the breast will be almost exactly twice the incident dose given by those two fields because the fields are no longer entering and being scattered by water or wax or tissues. The dosage at the deeper part of the breast will be much lower than that estimated from the isotope curves. If bolus material is added so that full scattering is obtained, the dosage at all points becomes almost identical. It is essential to use bolus, and if that is not done it can cause an erroneous estimation of the actual dosage given.

Dr. Taylor (closing). We do not use preoperative roentgen therapy and think a tumor dose of 1,500 r, as suggested by Dr. Berven, is inadequate. We do not use postoperative roentgen therapy routinely but have tried preoperative and postoperative treatment in about 50 cases. We have never felt that it influenced our results in any way.

The question was asked whether there was any evidence that roentgen therapy, given for recurrent or inoperable disease, prolongs the life of the patient. The only study I am aware of, on that, was published by Dr. Greenough many years ago, in the first report from the American College of Surgeons when they first began to assemble cases from a large number of clinics. He plotted the survivors following radiation therapy for inoperable disease against the curves which Daland had originally made, of the disease in untreated cases, and found that the graph for survivors following radiation therapy coincided exactly with Daland's curves for untreated cases. He concluded, therefore, that radiation therapy, although it improved the patient's comfort and frequently healed up ulcerations and otherwise was a very markedly beneficial palliative procedure, did not prolong the patient's life. To the best of my knowledge, there have been no further studies contributing directly to that problem.

The question was asked whether radiation castration can be shown to be beneficial as a prophylactic procedure following radical mastectomy or associated with radical mastectomy in operable cases in women before the menopause. I made a study on that several years ago in which we carried out an artificial menopause on 50 patients following radical mastectomy and compared them with a control series in which we had not carried out the radiation castration, and I was unable to establish that the prophylactic castration was of the slightest benefit in increasing the number of survivors or postponing the incidence of recurrence. That is quite different from the therapeutic use of radiation castration when recurrent disease establishes itself, especially skeletal metastatic disease.

Dr. Windeyer (closing). First, in answer to the questions which are posed to me, we do take biopsies in early cases in which we have doubted the diagnosis. There are obviously many cases, such as those which you have seen depicted here on the slides, in which there can be no reasonable doubt that one is dealing with a cancer and we do not take biopsies in those but we do get histological proof of them. I am not suggesting that our method of preoperative irradiation does sterilize the growth completely in all cases, but as I tried to point out before, I still believe that there is value in doing it even though there are demonstrable cancer cells which are also demonstrably damaged at the time of operation.

Dr. Haagensen poses the question which I think is the crux of this, as far as I am concerned, and that is the question of delay between irradiation and operation. He says it would take six months. We are doing it somewhere between three and four months and so far haven't got into any trouble with it. I do think that this is a very important point, this question of how long afterwards you are going to do any surgical procedure because there is an optimum time. If you delay too long you get into more trouble because you get more fibrosis.

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# AUTOMATIC ROENTGEN-RAY ROLL-FILM MAGAZINE FOR ANGIOCARDIOGRAPHY AND CEREBRAL ARTERIOGRAPHY*†

*By* CHARLES T. DOTTER, M.D., ISRAEL STEINBERG, M.D., *and* HAROLD L. TEMPLE, M.D.

NEW YORK, NEW YORK

VARIOUS devices for producing multiple roentgenographic records following the intravascular injection of radiopaque solutions have been devised, primarily for use in angiocardiography.[1–11] Although a few such apparatuses are commerciably available, most have been "home made," and as such have not received widespread application. In general, two principles have been followed: (1) rapid changing of cassettes, and (2) rapid photographic recording of roentgenoscopic images. The former is an inefficient method since it involves the shifting of heavy cassettes between each exposure. As a result, the interval between exposures has been longer than desirable and the maximum number of exposures limited by spatial considerations. In addition, apparatus capable of moving the weight of several cassettes has been of necessity heavy and not maneuverable. The photoroentgen method, while capable of producing a virtually unlimited number of exposures, has been hampered by the limitations of small film size and the distortion resulting from short target-screen distances. Its most valuable application is considered to be in the hospital where occasional angiocardiographic study is contemplated and where the equipment may be employed both for angiocardiography and for routine chest photofluorographic examinations.

It was felt that the ideal apparatus would consist of a roll-film magazine in which only the essential element—the roentgen-ray film—would be transported. The device should be light weight and maneuverable so as to be adaptable to upright and prone angiocardiography as well as intracranial arteriography. It should be so designed as to allow the use of the standard 6 foot target-film distance and standard roentgenologic equipment. With the cooperation of the Fairchild Camera and Instrument Corporation, such an apparatus has been devised and employed. This work has paralleled the efforts of Scott in St. Louis who employed a modification of the Fairchild 9 inch aerial camera magazine in conjunction with a self-cocking high-speed Bucky grid.[11]

FIG. 1. Fairchild automatic roll-film magazine viewed from behind, cover plate in place.

The magazine as employed by us is mounted upon a motor base plate which in turn is attached semi-permanently to a roentgen-ray table or other suitable support. The magazine (Fig. 1) is snapped into and out of the base plate for film loading and unloading in the darkroom.

* From the Department of Radiology of The New York Hospital-Cornell Medical Center.

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An easily removable cover protects two film spools, each of capacity to hold 75 feet of film 9½ inches in width. Two high-speed intensifying screens and a moving parallel grid are mounted on the front of the magazine and sheet lead protects the film supply from undesired exposure. A meter records the total number of films exposed. The magazine is equipped with a handle for easy carrying and weighs only 30 pounds, fully loaded, a weight equivalent to that of three 14 by 17 inch standard cassettes. Loading and unloading is no more complicated than the similar operation on an ordinary roll-film camera.

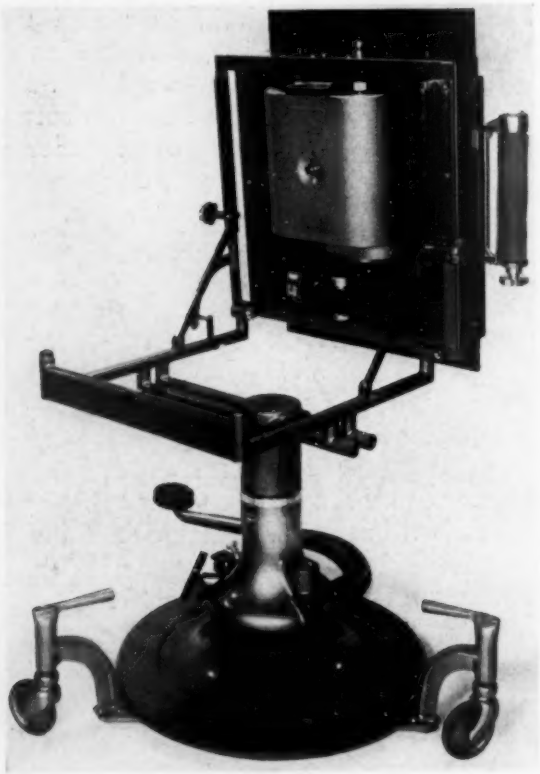

FIG. 2. Magazine mounted on motor base plate which is attached to Philips pedestal. Motor may be seen below magazine.

The motor base plate consists of an aluminum plate behind which are mounted a 1/15 horsepower electric motor with reduction gears, and the terminals for connecting electric leads. The outer dimensions of the motor base plate are 23 by 21¾ inches. With the magazine locked in place, the depth of the entire unit is 8 inches, and the weight is 49 pounds.

When the motor circuit to the magazine is closed from the roentgen-ray control panel the film is advanced 10 inches, then stopped by a clutch mechanism. A pressure plate sandwiches the film between the intensifying screens (which are mounted on felt pads) and the circuit to the roentgen-ray timer is closed, activating the roentgen exposure. The screens then are separated and the cycle is repeated every 0.5 second as long as motor current is supplied. During motor operation which is continuous, the parallel grid is kept in horizontal oscillation. A stationary fixed focus grid may be substituted for the moving parallel grid and is of particular use during intracranial arteriography.

We have employed the roll-film magazine mounted on a Philips pedestal Bucky stand (Fig. 2) allowing almost unlimited positioning and facilitating vertical or prone angiocardiography, intracranial arteriography, special studies during cardiac catheterization and cardiovascular visualization in the experimental animal (Fig. 3). A stretcher may be positioned over the magazine for prone angiocardiography and abdominal aortography. The device has afforded high quality, clearly defined roentgenograms in each application.

The duties of the technician during angiocardiography are simple. The magazine is actuated by a single control button and operation is automatic as long as the switch is held closed. The magazine may be run continuously for an entire cycle of contrast substance through the thorax. It may be run continuously during any selected period or periods of time or single exposures may be made at will. It has been convenient to operate the magazine during the first three seconds following the beginning of injection (obtaining studies of the right heart with its associated veins and arteries) and during the period of left heart opacification (between 7 and 10 seconds in the normal). A present, a 100 kv.(peak)

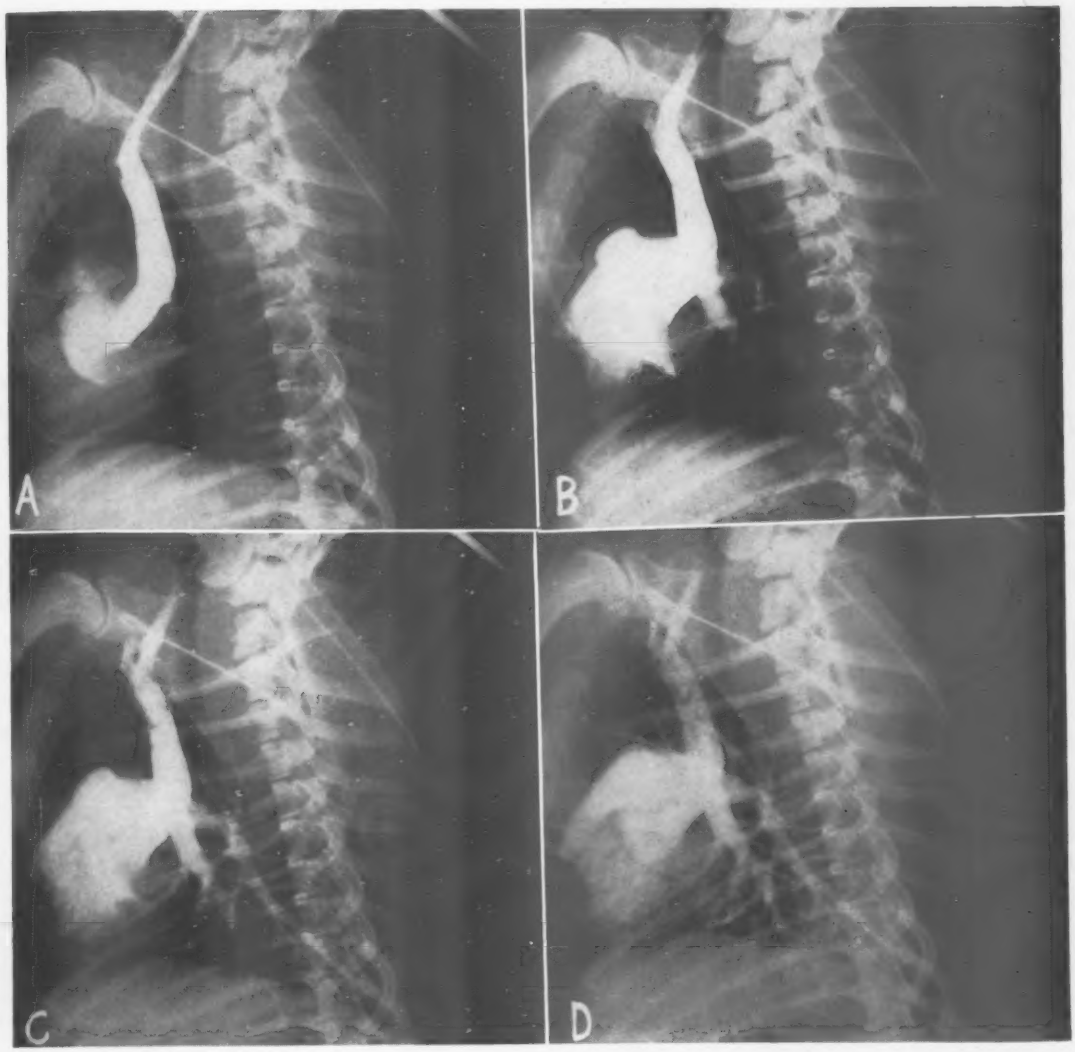


Fig. 3. Angiocardiographic study of right heart filling in dog, left anterior oblique projection. *A*, 0.5 second after beginning of injection. *B*, 1.0 second after injection. *C*, 1.5 seconds after injection. *D*, 2.0 seconds after injection. All structures are normal.

rotating anode tube is operated at 200 milliamperes. Exposure time of 1/10 second is used at a kilovoltage suited to the projection employed and the size of the patient. In the near future, modifications in timing apparatus now being made will allow 1/60 second exposures at 500 ma. All angiocardiography is done at 6 foot distance in the interest of uniformity and to minimize distortion. Intracranial arteriography and abdominal aortography is performed at 40 inch distance using a moving fixed-focus grid.

Actual measurements made with an ionization chamber reveal that the patient receives a total of 4.5 roentgens (average) during a twenty-four exposure run. This is considered to be within safe limits. The amount of radiation received by the doctor making the injection (protected by a long apron or a lead screen) falls within the allowable limits for such exposure. Calculation of heat units indicates that a run of twenty-four consecutive exposures during a 12 second time does not exceed the tube limits (rotating anode tube).

Double emulsion du Pont roentgen-ray film made up by the manufacturer in 75 foot rolls has proved satisfactory in our experience, as have other standard brands of roentgen-ray films. Recommended time-temperature development is carried out using the Fairchild X-Ray Film developing unit. Following developing, fixing and washing, the film may be conveniently dried as a long strip draped over hangers in the film dryer.

The resultant exposed films measure $9\frac{3}{16}$ by $9\frac{7}{16}$ inches in size. It would be desirable to have a slightly larger film size than is at present available, but by roentgenoscopy of the patient prior to angiocardiography, satisfactory positioning may be easily obtained.

It is believed that this magazine presents the best available means of angiocardiographic recording and that eventual refinements will be directed along the principles it employs. The unit is commercially available. Other planned applications of the apparatus include uterosalpingography, special studies of gastrointestinal motor function and electrocardiographically controlled contrast studies of cardiac chamber volume and wall thickness. The small size of the unit will allow the use of two tubes and two magazines in order to obtain simultaneous recording in two projections. Further modes of application are expected to widen the usefulness of this device beyond the scope of this initial preliminary report.

The New York Hospital
525 East 68th St.
New York 21, N.Y.

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# GENERALIZED PROGRESSIVE SCLERODERMA*

## REPORT OF AN INSTANCE OF ESOPHAGOSCOPIC PERFORATION OF THE ESOPHAGUS WITH DESCRIPTION OF THE ROENTGENOLOGICAL AND NECROPSY FINDINGS

*By* GERHART S. SCHWARZ, M.D.†
CLIFTON SPRINGS, NEW YORK
*and*
OLAF K. SKINSNES, M.D., PH.D.‡
NEW YORK, NEW YORK

FEW instances of sclerodermatic stricture of the esophagus correctly diagnosed roentgenologically and proved by necropsy have been reported. Lindsay *et al.*[6] state, in their recent review of the literature, that postmortem examinations of this lesion have been reported in only 3 instances. Olsen *et al.*,[9] in a later review, which includes the preceding 3 reports, found 8 cases with necropsy findings described. All revealed pathological changes in the esophagus attributable to scleroderma. No definite reference was made to the presence or absence of stricture, however. An additional report has since been added by Goetz.[1] The following report is presented as an additional necropsy study because of its roentgenological interest centering about a complicating esophageal perforation, the true nature of which was revealed only at autopsy.

### CASE REPORT

*Clinical History*. W. S., a married woman, aged sixty-seven, prominent in political activities and of Irish extraction, was admitted to the University of Chicago Clinics on January 1, 1945, five years following a diagnosis of Reynaud's disease which was based on progressive ulceration of the fingers. In the interim she had been active and well save for this affliction which was not incapacitating. Six weeks prior to her final hospitalization she began to note shortness of breath associated with the eating of solid foods and relieved by regurgitation. She also noted difficulty in swallowing, retrosternal pain, coughing, and frequent regurgitation of gastric contents without nausea. These symptoms persisted and her physician reported roentgenoscopic and roentgenologic evidence of lower esophageal stricture with proximal dilatation. His report did not mention any upper esophageal lesion. Further examination, by esophagoscopy with biopsy, performed on December 19, 1944, two weeks prior to terminal hospitalization, was reported as suggestive of epidermoid carcinoma of the esophagus with associated inflammation. These biopsy sections were later reviewed at the University of Chicago Clinics and deemed non-neoplastic. The only anesthetic used at esophagoscopy was a spray. Following this procedure the patient experienced slight swelling and soreness of the throat and increased difficulty in swallowing for some days.

At the first roentgen examination in the University Clinic, on January 2, 1945, amputation (probably spontaneous) of the terminal phalanx of the second digit of the left hand and osteo-arthritis involving many digits of both hands were noted (Fig. 1). Barium study of the esophagus by roentgenoscopy and roentgenography revealed a fusiform narrowing of its lower third and dilation of its middle portion (Fig. 2 and 4). Sclerodermatic stricture of the esophagus was diagnosed on the basis of the smooth fusiform appearance of the esophageal stricture and its association with the digital lesions.

The roentgen studies also disclosed a 10 cm. long, spoon-shaped pouch lying dorsal to the upper third of the esophagus (Fig. 3 and 4).

* From the Division of Roentgenology and the Department of Pathology, the University of Chicago, Chicago, Illinois.
† Department of Radiology, Clifton Springs Sanitarium and Clinic, Clifton Springs, N. Y.
‡ Now Department of Pathology, Cheeloo University, Foochow, Fukien, China.
Acknowledgment is gratefully made of the permission of Dr. D. B. Phemister to publish this case, of the helpful suggestions of Drs. P. C. Hodges, J. R. Lindsay, E. M. Humphreys, and P. R. Canon, and of the careful work of Miss R. C. Winkler in the preparation of the histopathological sections.

FIG. 1. Roentgenogram of the patient's left hand. There is auto-amputation of the distal half of the distal phalanx of the second digit and minor osteoarthritic changes are seen in several of the joints.

This pouch filled with barium when the patient tipped her head back while swallowing. This act was invariably accompanied by coughing. Communication between the pouch and the esophagus was by a narrow isthmus not more than 5 mm. wide which lay at the level of the sixth cervical vertebra. The location of the pouch and the smoothness of its walls suggested the diagnosis of a diverticulum, possibly of Zenker's type, despite a suggestion by the referring service to the effect that it might represent esophageal perforation by esophagoscopy with leakage of barium into the soft, retro-esophageal tissues. Subsequent roentgen studies of a coincident pulmonary infection performed five days later indicated that the barium had escaped from the pouch. This complete disappearance of the contrast material was interpreted as additional indication of the diverticular nature of the lesion. Under sulfadiazine and penicillin therapy the pulmonary infection subsided and the leukocyte count dropped from a previous high of 20,500 to 9,500 by the day of operation. A urea clearance test indicated renal function of 46 per cent of the mean normal ($U/B\sqrt{V}=25.8$), but other laboratory tests were negative. At a preoperative roentgen study of the esophagus on January 24, 1945, barium failed to enter the previously seen pouch. It was assumed that this failure to visualize the lesion twenty-two days after it was first seen indicated that its narrow isthmus had closed.

Diffuse inflammation of the esophagus up to the level of the lung hila was noted on the thirty-sixth hospital day when a transthoracic, side-to-side esophagogastrostomy was performed to relieve the patient's difficulty in swallowing. On the first postoperative day she vomited and aspirated gastric contents. Her temperature rose to 39° C. and remained at about this level thereafter. On the second postoperative day she was oliguric and her reduced blood pressure necessitated a blood transfusion. No reaction was noted but subsequently she became slightly icteric. Signs of aspirative bronchopneumonia, were present. On the third day she again aspirated vomitus and died early on the fourth day with continued evidence of respiratory distress despite chemotherapy, bronchoscopic

FIG. 2. Fusiform stricture of the lower third of the esophagus demonstrated on the roentgenogram.

aspiration and other therapeutic and supportive measures.

*Necropsy Findings* (Autopsy 6426). Postmortem examination was performed six hours after death. The skin was generally fair and soft but slightly icteric above the level of the navel. The body was well nourished. The index finger of the left hand lacked the terminal phalanx and the overlying skin was taut, puckered and indurated. That covering the terminal phalanges of the other fingers showed similar induration but no ulceration. The finger nail of the fourth right digit was loosened and at its base new nail growth was evident. Histopathologically the skin of the chest and abdomen was not remarkable. That of the sclerotic finger tips displayed moderate collagenous sclerosis of the corium with hyalinization of the collagen bundles. A few of the underlying arterioles contained antemortem thrombi and the epidermis was thickened and slightly hyperkeratotic.

Lying at the level of the cricoid cartilage on the posterior wall of the esophagus was a 3 mm. deep outpouching which, on microscopic examination, was seen to extend through the

Fig. 3. Cervical esophagus at the first roentgenological examination. The retouched roentgenogram shows the spoon-shaped, retro-esophageal pouch filled with barium and communicating with the esophagus by a narrow neck at the level of $C_5-C_6$. Its contours are smooth.

Fig. 4. Left lateral view of the entire esophagus obtained at the first roentgenological examination. Patient standing. Upper portion slightly retouched. The upper end of the neck of the retro-esophageal pouch appears as in Figure 3. The lower end appears to have a second communication with the esophagus which may be due to an overlapping of both structures since there is no assurance that this represents a true profile view. Retropharyngeal air appears to be present above the neck of the pouch or pseudo-diverticulum. The esophagus is dilated above the distal stricture and contains air and food particles.

FIG. 5. Esophagus and stomach showing esophageal stricture, esophagogastrostomy, esophageal leukoplakia, upper esophageal outpouching, and lower esophageal outpouching.

tunica muscularis and to end blindly, being lined with squamous epithelium (Fig. 5 and 6). Five and a half centimeters directly below it there was a similar but slightly more shallow outpouching having similar microscopic characteristics but extending only to the tunica muscularis (Fig. 5 and 7). Grossly the retro-esophageal connective tissue lying between these two outpouchings was thicker and denser than the peri-esophageal tissue found elsewhere. Sections through this cord of tissue after fixation disclosed a small flattened lumen beginning at about the level of the upper outpouching and extending downward toward the lower outpouching for about 2.5 cm. Microscopically, in multiple sections, this lumen was found to lie entirely outside of the tunica muscularis (Fig. 8). It was collapsed, having a greatest diameter of about 7 mm. Its wall was composed of granulation tissue in which food particles of vegetable origin and foreign body giant cells were scattered. A few, relatively large blood vessels lay perilously close to the lumen. This pseudo-diverticulum was completely devoid of epithelial lining save for a small focus at its upper pole where there was a discontinuous, two cell thick layer of squamous epithelium. This lay close to the epithelium of the upper outpouching but it was not possible to demonstrate any direct connection between the two. The lumen of the pseudo-diverticulum contained a small amount of amorphous, protein-like matter, numerous bacterial colonies and

FIG. 6. Histpathological section of the upper esophageal outpouching illustrating its close proximity to the upper portion of the pseudo-diverticulum. There is extensive surrounding fibrosis. Heidenhain's modification of Mallory's connective tissue stain. ×23.

Fig. 7. Histopathological section of the lower esophageal outpouching. There is intense surrounding fibrosis and disruption of the muscular coats. The pseudo-diverticulum site is represented by dense fibrous tissue lying external to the tunica muscularis. Heidenhain's modification of Mallory's connective tissue stain. ×27.

occasional inflammatory cells but no desquamated epithelial cells. The upper esophageal outpouching was connected to the lumen of the pseudo-diverticulum by a dense band of collagenous fibrous tissue extending through the tunica muscularis (Fig. 6). In its lower portion the pseudo-diverticulum was obliterated by fibrous tissue and its connection with the lower esophageal outpouching was represented by a dense band of fibrous tissue (Fig. 7).

Twelve and a half centimeters above the cardia the esophageal epithelium, which above this level showed only microscopic foci of leukoplakia, began to show clear-cut leukoplakic thickening. Grossly and microscopically this became progressively more pronounced toward the lower esophagus achieving a thickness three to four times that prevalent in the upper third. One millimeter wide erosions extending in all directions, but predominantly vertically, divided the leukoplakic epithelium into islets of various sizes and shapes having diameters averaging roughly 5 to 7 mm. The greatest esophageal circumference of 6.5 cm.

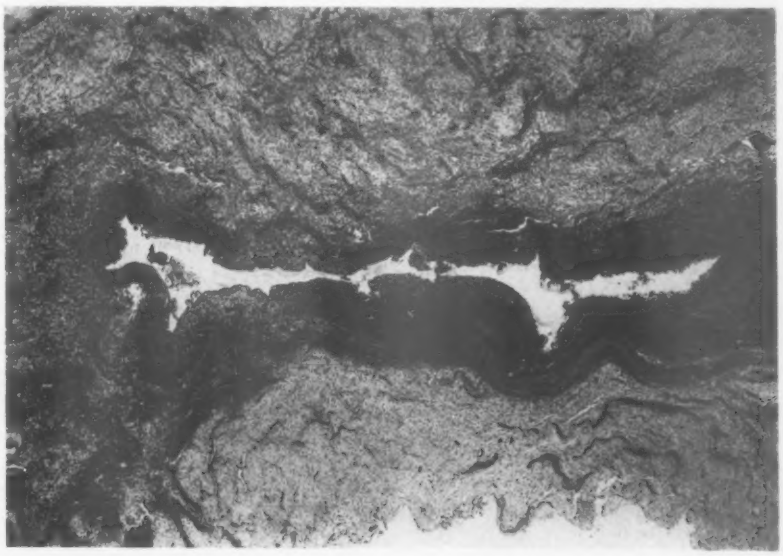

Fig. 8. Histopathological section of the pseudo-diverticulum illustrating its granulation tissue wall, its close proximity to a large vein, and the only area of epithelial lining found in the lesion. This epithelial layer was present in the upper portion of the pseudo-diverticulum, was discontinuous and presumably arose from displaced esophageal epithelium. Hematoxylin-phloxin stain. ×32.

lay 7 cm. above the cardia. The terminal esophagus displayed a 2.5 cm. long stenotic passage having a circumference of 2.3 cm. (Fig. 5). Just above this stenotic passage there was a side-to-side esophagogastrostomy, the suture lines of which showed good healing save for a 4 mm. opening lying posteriorly in friable, discolored, necrotic tissue and communicating through the posterior mediastinum with an extensive fibrinopurulent left pleural empyema cavity.

FIG. 9. Histopathological section of the esophagus illustrating the esophageal leukoplakia, epithelial erosion, submucosal fibrosis and fibrous atrophy of the inner circular layer of the tunica muscularis. Hematoxylin-phloxin stain. ×82.

Microscopically the upper esophageal epithelium showed occasional minute intraepithelial acute abscesses and eroded foci with underlying acute focal inflammatory changes. The progressively increasing leukoplakia in the lower esophagus was increasingly frequently interrupted by more extensive areas of ulceration with underlying acute inflammation. The muscularis mucosae gave the impression of being slightly hypertrophic, especially in the lower esophagus, but it was repeatedly disrupted by the inflammatory changes underlying the epithelial erosions, and by the submucosal fibrosis. The submucosa was characterized by dense hyalin fibrous sclerosis with decreased cellularity, more marked in the lower portion of the organ. The tunica muscularis showed remarkable atrophy of the smooth muscle fibers and encroachment of fibrous tissue at the interdigitation of the smooth and striated muscle fibers in the upper esophagus. Similar changes were not noted in the striated muscle. The inner circular layer of smooth muscle, in contrast to the outer longitudinal layer, was generally atrophic throughout the esophagus and displayed marked fibrous encroachment (Fig. 9). At the cardio-esophageal stricture the epithelium was largely sloughed and the immediately underlying tissue showed subacute inflammatory changes characterized by lymphocyte and plasma cell infiltration. The submucosa revealed extremely dense fibrous sclerosis with hyalinization and disruption of the muscularis mucosae and extension of the fibrotic sclerosis into the tunica muscularis. The included arterioles were sclerotic and sclerosis of the smaller arteriolar radicals was prominent throughout the lower esophagus.

Elsewhere the alimentary tract was not remarkable.

Increased fibrosis was evident in many other areas of the body though the homogenization frequently described as a characteristic of sclerodermic fibrosis was not noted. The renal capsule displayed striking fibrosis with little cellularity and the glomeruli showed fine disseminated intercapillary fibrosis not unlike that seen in the intercapillary sclerosis associated with diabetes save for the lack of formation of hyalinized balls of connective tissue. The epicardium showed similar hyalinized fibrosis with decreased cellularity far antedating the overlying acute fibrinous pericarditis, and the myocardium contained scattered foci of hyalin fibrosis. Atrophic muscle fibers and arterioles were often included in these areas of fibrosis though the fibrosis was not invariably associated with blood vessels. The endocardium likewise showed occasional small foci of fibrous thickening.

In addition to the above findings and the evidences of the surgical procedures the anatomical diagnosis included the following: left

thoracic fibrinopurulent empyema, fibrinous pericarditis (non-hemolytic streptococci and *B. coli*), left pulmonary atelectasis, bilateral aspirative bronchopneumonia and bronchitis, myeloid hyperplasia remarkable for the relative increase in eosinophils.

## DISCUSSION

During the past few years it has become increasingly evident that running through the varied clinical and pathological pattern of generalized progressive scleroderma lies a basic sclerosing change in the connective tissue of as yet unknown etiology. Together with the knowledge that the varied symptomatology is to a large extent based on the localization of the process and its severity, greater attention has been focussed on the esophagus, as well as other portions of the alimentary system, as a not infrequent site of severe change. Despite this there have been few recorded opportunities for histopathological investigation of this change.[1,5,6,13,20]

The nature of the esophageal lesion responsible for the presenting symptoms was readily established antemortem in the instance here described. Roentgenologic interpretation of the esophageal stricture was not problematic. Its smooth contours, fusiform shape, and association with destructive terminal finger lesions suggested esophageal scleroderma. The necropsy findings of mucosal erosion, submucosal fibrosis, hypertrophy of the muscularis mucosae, fibrous atrophy of the inner layer of the tunica muscularis, and the marked leukoplakia confirmed the diagnosis of scleroderma (or progressive systemic sclerosis). The increasing severity of these changes in the distal portion of the esophagus lends support to the suggestion of Lindsay *et al.*[6] that these changes may be largely secondary to a primary disturbance of esophageal function leading to regurgitation of gastric contents with a resultant peptic esophagitis and gross anatomic changes. Esophageal leukoplakia is often seen in association with chronic esophagitis (Templeton)[19] and the progressively increasing severity of the lesion toward the cardia in this instance supports this concept. In view of the widespread tendency toward fibrosis evinced by this disease process, it may be that the marked esophageal sclerosis represents an exaggerated response to the chronic trauma of regurgitation, or on the other hand, the esophagitis may serve to provide a locus minoris resistentiae allowing increased local activity of whatever etiologic agent is involved.

The nature of the retro-esophageal pouch was more obscure. Its smooth contours and location were characteristic of a diverticulum, possibly of Zenker's type, but it was recognized that it is unusual for an upper esophageal diverticulum to be so long and narrow. Usually they are rounded and do not dissect along the esophagus. The reported failure to visualize the lesion on pre-esophagoscopic roentgenoscopy together with repeated failures to revisualize it on later examinations bespoke its temporary nature and suggested the esophagoscopic examination as being its traumatic cause. No statement has been found in the literature which mentioned failure of a subpharyngeal diverticulum to fill once it has been visualized. Such a possibility is conceivable should the diverticulum have as small a neck as that described in this instance since the opening could be occluded by food particles or mucus, or could possibly be strangulated by torsion. The absence of retro-esophageal emphysema spoke against a recent perforation. Possibly too much time elapsed between the time of injury and that of examination to allow demonstration of this sign. A solitary collection of air behind the pharynx was, probably correctly, interpreted as having accumulated in the upper portion of the pseudo-diverticulum.

Recognition of traumatic perforation of the esophagus by extravasation of contrast material into the mediastinum is rare. Most reports have concerned a single case often included in a series of perforated esophagi recognized by other means or by other roentgen signs.[4,8,10,15,17] One reason for this

is the hesitation with which barium is given in such instances, the objections being largely surgical (e.g., fear of obscuring esophagoscopic or operative fields, interference with the healing of mediastinal abscess due to the presence of foreign body material). Some authors,[3,7,10,15,18] however, do not raise any objection to the procedure.

The difficulties of esophagoscopy in patients with scleroderma are not sufficiently well recognized. It is becoming increasingly apparent from instances such as this that esophagoscopic procedures in these patients are safest when carried out under general anesthesia.

A case reported by Robinson[14] is similar to that here reported in the nature of the perforation. A barium filling, retro-esophageal pouch was observed in the cervicothoracic region of a young woman nine days after esophagoscopy for the removal of a swallowed bone. The pouch had ragged, scalloped borders. Its size, shape and location were almost identical with those of the present report. A week later no barium rest could be visualized in the region and repeated attempts to refill the pouch with barium failed. Following esophagoscopy chest symptoms and a mild fever developed but a month later the patient recovered completely without surgical intervention.

In the presently reported instance the abscess had apparently emptied into the esophagus spontaneously through the lower perforation, leaving as a scar a small esophageal outpouching, and thus imitating well the surgical treatment for periesophageal mediastinitis inaugurated by Seiffert[16] which consists of longitudinal slitting of the gullet through the esophagoscope.

## SUMMARY

Roentgenologic and necropsy findings in an instance of lower esophageal stricture associated with digital lesions and diagnosed as esophageal scleroderma are reported. A retro-esophageal pseudo-diverticulum occurring as a result of esophagoscopic examination is likewise described and illustrated. The differential diagnosis and implications of the perforation are discussed.

Gerhart S. Schwarz, M.D.
Clifton Springs Sanitarium and Clinic
Clifton Springs, N.Y.

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# ULCER ASSOCIATED WITH DIAPHRAGMATIC HERNIA*

*By* GLENN F. MILLER, M.D., *and* HOWARD P. DOUB, M.D.
*Department of Roentgenology, Henry Ford Hospital*
DETROIT, MICHIGAN

CAREFUL roentgenographic examination of large numbers of the general population has disclosed the fact that diaphragmatic hernia is a common anatomic abnormality. The roentgen characteristics of this condition have long been familiar, and the symptoms and signs constitute a fairly definite clinical syndrome. In many cases the hernia is small and is regarded merely as an incidental finding, without clinical significance. In other cases, however, especially where the hernial sac is large, there is a strong probability that it is of distinct importance, and a painstaking roentgenoscopic and roentgenographic study is indicated to evaluate its relation to the clinical picture.

The discovery of a small series of gastric ulcers associated with diaphragmatic hernia has raised the question of the incidence of this association, and has suggested that it may be more frequent than was previously thought. It is believed, also, to constitute a definite problem from the point of view both of symptoms and treatment.

The term diaphragmatic hernia is commonly used to designate the protrusion of any of the abdominal contents through an abnormal opening in the diaphragm or through an enlargement of the esophageal or other normal hiatus. Three main groups are usually recognized: (*a*) congenital, due to an embryologic deficiency, usually without an enclosing sac; (*b*) acquired, in most cases as a result of dilatation or relaxation of a hiatus in the diaphragm, and when occurring through the esophageal hiatus, usually provided with an enclosing sac; (*c*) traumatic. Some authors would include this last group with the acquired hernias, but others believe it should be considered separately, comprising those cases due to accident, operation or rupture secondary to subdiaphragmatic abscess. Hume[7] believed that thoracic stomach with short esophagus should not be included in the foregoing classification, since the stomach in such cases has never been an abdominal organ and herniation does not enter into the picture. Eventration may also be excluded, as in this condition the stomach remains below the diaphragm.

In our study of 290 cases of diaphragmatic hernia at the Henry Ford Hospital, we have found herniation through the esophageal opening to be the most frequent type in the adult, an observation in accord with that of Harrington and Kirklin,[6] and others. These hernias are most often non-traumatic and have an enclosing sac. Åkerlund[1] called them "hiatus hernias" and divided them into three groups including the short esophagus cases. His classification is as follows: (*a*) congenital short esophagus with partial or complete thoracic stomach; (*b*) esophageal hiatus hernia with an esophagus of normal length which does not form a part of the hernia, that is, paraesophageal hernia, and (*c*) hiatus hernias not included in (*a*) and (*b*).

In 1929 Collier *et al.*,[2] in a review of the literature, found only 3 cases of diaphragmatic hernia associated with a chronic gastric ulcer. The first case, a description of which they include, was published by Bright in *Guy's Hospital Reports* in 1836. The patient was subject to attacks of sudden dyspnea and indigestion, and lying on the left side frequently caused vomiting. Death resulted from exhaustion after a long period of vomiting and dyspnea. Autopsy revealed a diaphragmatic hernia, with the stomach filling the lower portion of the thoracic cage, and two or three deep

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chronic ulcers on the lesser curvature. The second case was reported by Hoffmann, of Heidelberg, in 1917 and was believed to be traumatic in origin, following a heavy fall resulting in several fractured ribs. Six weeks after this accident the patient suffered from indigestion for the first time and vomited dark clots. There ensued a twelve year period of vomiting and indigestion which became progressively severe and frequent, with a hemoglobin of 55 per cent at the time of death. A diaphragmatic hernia was found at autopsy, with an ulcer on the lesser curvature side of the stomach. The third report was by Key, of Stockholm, in 1924, who apparently was the first to demonstrate roentgenographically a case of diaphragmatic hernia associated with ulcer which was later proved at operation. To these cases Collier and his associates added 2 more which they demonstrated roentgenographically. In each instance there was a left diaphragmatic hernia containing about one-third of the stomach and showing a large crater on the lesser curvature, just below the diaphragm where it was constricted by the hernial orifice. Both cases were proved at autopsy.

Truesdale,[13] in 1932, found listed in the literature 17 cases of ulcer of the herniated stomach and reported one of his own, bringing the total to 18. His analysis of this series disclosed that 10 occurred in males and 8 in females, the age ranging from nineteen to sixty-eight years, with an average of forty-four plus. In 15 of the cases the hernia was of the esophageal hiatal type and in 14 of these an ulcer was present on the lesser curvature of the stomach at the hiatal narrowing. There was one hernia through the orifice for the vena cava and one through the foramen of Bochdalek. The remaining case was one of congenital short esophagus. The type of ulcer varied from a small niche to multiple perforating lesions. In one case the ulcer eroded a branch of the pulmonary artery causing a fatal hemorrhage.

Four cases have appeared since Truesdale's review, bringing the total to 22. Sangster,[10] in 1936, presented a case in which at autopsy there was found a hernia through the tendinous portion of the diaphragm into the left pleural cavity, containing the transverse colon, stomach, and 25 cm. of jejunum. On the lesser curvature of the stomach was an ulcer which had perforated. In 1941 a case was reported by Frank and Hamilton[4] in which the defect was just to the left of the esophageal hiatus and the hernia contained a portion of the stomach, with a large penetrating gastric ulcer, and a part of the transverse colon. Two other cases, of the hiatal hernia type with an ulcer present in the area of narrowing, were reported by Steiner[12] in 1946.

Like Åkerlund, we have regarded the congenital short esophagus with thoracic stomach not as a separate entity but as a subdivision of hiatus hernia, to which it is related embryologically, the rate of descent of the stomach during the formation of the diaphragm being the determining factor. According to Shanks,[11] the rate of descent determines whether the stomach may be trapped by the diaphragm and become partially thoracic in location or, if the lag is slighter, may produce only a slight enlargement of the esophageal orifice.

From a review of the literature we assembled 38 cases of congenital thoracic stomach with an ulcer present in the short esophagus at its point of junction with the cardia. Seven cases of esophageal ulcer associated with a gastric hiatus hernia were also found. The age range in this collected series was from forty-five to sixty-eight years, with the exception of one case occurring in a three year old child. The sex incidence was approximately equal. Six cases were demonstrated roentgenographically and in 37 there was some indication of gastric bleeding, hematemesis, occult blood in the stools, tarry stools, or anemia.

Ulcers occurring in the short esophagus associated with the thoracic stomach have generally been conceded to be the result of the action of acid gastric juice on the stratified squamous epithelium of the esophagus, which cannot withstand its eroding action.

The acid gastric juice reaches this area by regurgitation, explained by Dick and Hurst[3] as being due to the loss of the valvular mechanism normally present at the cardia when it is situated in the abdomen. The action of this gastric regurgitation is abetted by the presence of islets of gastric mucous membrane, which have been found in the lower end of the esophagus by Jackson.[8]

Ulcers which occur in conjunction with true hiatal hernias are considered by Rude,[9] Truesdale,[13] and others, to be primarily the result of irritation and trauma to the stomach wall by the constricting action of the hiatal orifice, which leads to congestion, varicosities, disturbance of the arterial blood supply, and eventually to erosion and active ulcer. Other factors are the strain produced in the act of vomiting and the presence of the active secreting glands, which are more abundant on the lesser curvature side of the stomach. These observations appear to be borne out by Harrington's[5] series, in which he has found all stages of involvement from superficial erosion of the gastric mucosa to definite ulcer formation with a well defined crater.

The symptomatology of ulcer associated with hiatal hernia is dependent upon the extent of the herniation, the degree of constriction produced by the hernial opening, and the amount of embarrassment to the thoracic contents. A few cases have been reported in which the patient exhibited typical ulcer symptoms, but we are inclined to agree with Truesdale[13] and others in the belief that such instances are in the minority. For the most part, the ulcer has been unsuspected, being found only at operation or autopsy. In a number of instances autopsy revealed an ulcer of considerable size which had been overlooked even at operation. One finding which has impressed us strongly, however, both from our own cases and from a review of the cases reported by others, is that clinical indication of gastrointestinal hemorrhage is almost invariably present. This may be in the manner of frank hemorrhage, which, according to Harrington,[5] is usually indicative of severe incarceration of the stomach, or as tarry stools, ocult blood in the stool, or secondary anemia.

In our own series of 6 cases of ulcer associated with esophageal hernia, demonstrated roentgenologically, the age range was from twenty-eight to sixty-five, with an average of fifty plus. Three of the patients were men and 3 women. In all but one there was a tendency toward obesity. In only one case was the diagnosis made clinically. All but one patient exhibited signs indicative of gastric bleeding. Of our cases of diaphragmatic hernia uncomplicated by ulcer 65 per cent showed some indication of hemorrhage.

We have found roentgenoscopy in both the upright and prone positions advisable, followed by corresponding roentgenographic studies. In the prone position, right anterior oblique views have proved most useful, as the barium is held in the cardia and the esophagus. It was sometimes necessary to lower the head of the table slightly and palpation was occasionally required.

## CASE REPORTS

CASE 1. S. F., male, white, aged forty-one, travelling salesman, complained of recurrent epigastric pain over a period of five years. It was irregular in character, was not definitely related to food, but was aggravated by alcohol. Tarry stools had been passed on several occasions. The guaiac test for occult blood was 4 plus. A borderline anemia was present.

Roentgenography revealed a diaphragmatic hernia, with the antrum and cap in the thoracic cavity. The cap was deformed, and on the lesser curvature at the point of narrowing, where the stomach passed through the opening of the diaphragm, was an ulcer (Fig. 1). A phrenic crushing was performed on the left and the hernia was repaired. The stomach was not opened at the time of operation. A postoperative roentgen study showed reduction of the hernia to be almost complete, with only a suggestion of a small pocket projecting through the hiatal opening (Fig. 2). The ulcer crater on the lesser curvature side of the stomach was still demonstrable roentgenoscopically and on the

films. The patient later was transferred to a Veterans Hospital and the case could not be followed further.

Case II. A. A., female, white, married, aged twenty-eight, had suffered from cardiospasm since the age of fourteen. Roentgenograms showed this to be rather advanced, with marked dilatation of the esophagus (Fig. 3).

Fig. 1. Case I. Diaphragmatic hernia with antrum and cap in the thoracic cavity. Deformed cap and gastric ulcer on lesser curvature of the stomach at the hiatus.

The condition was corrected surgically at the age of thirty. Six months later the patient complained of pain in the lower portion of the chest, which was aggravated by meals. She gave a history of coffee-ground vomitus and tarry stools on several occasions. Laboratory reports showed a 4 plus guaiac reaction in the stool and a severe secondary anemia, with hemoglobin of 3.4 gm. Roentgenographically a portion of the stomach appeared to be pulled up through the esophageal hiatus and an ulcerative lesion was demonstrable at the esophageal orifice where the upper end of the stomach passed through (Fig. 4). On esophagoscopy a small ulcer was seen a few centimeters above the stomach, in the esophagus. The patient later moved from the city and contact with her was lost.

Fig. 2. Case I. Postoperative roentgenogram with practically complete reduction of the hernia. The ulcer crater on lesser curvature side of the stomach still visible.

Fig. 3. Case II. Advanced degree of cardiospasm with marked dilatation of the esophagus.

FIG. 4. Case II. Postoperative roentgenogram; a portion of the stomach appeared to be pulled up through the esophageal hiatus with an ulcerative lesion at the esophageal orifice.

CASE III. M. S., male, aged sixty-two, had an esophageal hiatus hernia diagnosed a year previous to the onset of epigastric distress. At the time of roentgen examination there was not a definite history of ulcer, and there were no clinical findings indicative of gastrointestinal bleeding. A large hiatal hernia with an ulcer pocket on the lesser curvature side of the stomach, near the point of its herniation through the diaphragm, was visualized roentgenographically and roentgenoscopically. The patient responded well to medical management but unfortunately progress roentgenograms were not obtained.

CASE IV. P. B., white widow, aged sixty-five, was suspected clinically of having metastatic carcinoma of the lower bowel. The guaiac test of the stool was 4 plus upon several occasions. Roentgenographically a large hiatal hernia was seen, with most of the stomach in the chest cavity and an ulcer at the point of narrowing (Fig. 5). A second examination showed the same picture. A year later the ulcer was no longer

FIG. 5. Case IV. Large hiatal hernia with most of the stomach in the chest cavity and an ulcer at the point of narrowing.

FIG. 6. Case IV. At examination a year later the ulcer was no longer demonstrable but the hernia was still present.

Fig. 8. Case vi. Diaphragmatic hernia with a diverticulum in the cardiac end of the stomach as well as an ulcer at the hiatal opening.

demonstrable but the hernia was still present (Fig. 6).

Case v. W. S., white male, aged sixty-four, a retired lumberman, had a previous diagnosis of diaphragmatic hernia. On clinical examination, the impression was diaphragmatic hernia with ulcer. The laboratory findings showed a severe secondary anemia. Roentgenographically a hiatal hernia was demonstrated, with a large ulcer pocket on the lesser curvature side of the stomach, just above the diaphragm opening (Fig. 7). Myocardial failure ensued and at autopsy the ulcer was found to have penetrated the stomach wall and to be walled off by peripancreatic fat.

Case vi. I. P., housewife, aged fifty, gave a five year history of dull epigastric distress which had gradually become worse, with episodes of pain associated with nausea and vomiting. On two occasions there was coffee-ground vomitus and the stool gave a 4 plus guaiac reaction. On three different occasions roentgenograms revealed a diaphragmatic hernia with what we believe to be a diverticulum in the cardiac end of the stomach, as well as an ulcer at the hiatal opening where the herniation occurred (Fig. 8). The patient was placed on strict medical management. Subsequent ex-

Fig. 7. Case v. Hiatal hernia with large ulcer pocket on the lesser curvature side of the stomach just above the diaphragm opening.

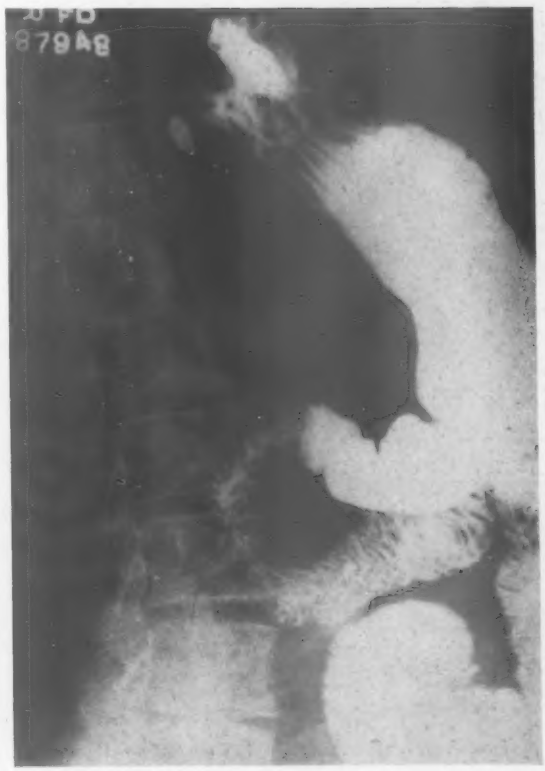

Fig. 9. Case vi. After medical management subsequent examination again showed the diverticulum but the ulcer pocket was no longer demonstrable.

amination again showed the diverticulum but the ulcer pocket was no longer demonstrable either roentgenoscopically or on the roentgenogram (Fig. 9).


## SUMMARY

The subject of diaphragmatic hernia has been briefly reviewed and the problem of ulceration occurring in connection with hiatal hernia and the congenital short esophagus with thoracic stomach has been discussed. Inclusion of the short esophagus with thoracic stomach as a subdivision of hiatal hernia is justified on embryologic grounds.

Twenty-two cases of gastric ulcer associated with hiatal hernia were collected from the literature and six new cases are reported. Such ulcers are attributed primarily to the constricting action of the hiatal orifice.

Thirty-eight cases of esophageal ulcer in patients with congenital short esophagus and thoracic stomach were discovered in the literature. Regurgitation of the acid gastric juice and its eroding action on the stratified squamous epithelium of the esophagus are believed to be the responsible factors in these cases.

It is probable that the occurrence of ulceration in conjunction with diaphragmatic hernia is more frequent than has been realized. Clinical symptoms of ulcer are often absent, though in practically all cases there has been some evidence of gastrointestinal bleeding. It is probable, however, that some of these cases are being missed roentgenographically, as a number of them have been discovered primarily at operation or at the postmortem examination. A careful roentgenologic study should be made for ulcer craters, especially in the narrowed area of the stomach where it passes through the esophageal hiatus.


Henry Ford Hospital
Detroit 2, Mich.

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## DISCUSSION

DR. ROSS GOLDEN, New York, N. Y. Drs. Miller and Doub have given an excellent review of ulcer in hiatus hernia. Bleeding from the mucosal surface of the herniated portion of the stomach can occur without peptic ulceration, but it seems probable that some small craters may be hidden among the enlarged mucosal folds. They mentioned the right prone position. In my experience, this is the best position for detecting small hiatus hernias, and is better than the supine Trendelenburg position with manual pressure on the epigastrium. This is probably due to the increased intra-abdominal pressure produced by the weight of the body on the abdomen.

VOL. 62, NO. 3

# RELATIVE INCIDENCE OF BONE LESIONS OVER A THIRTY-SEVEN YEAR PERIOD*

*By* SHERWOOD MOORE, M.D.
ST. LOUIS, MISSOURI

THE changing picture of disease has not engaged the attention of the medical profession as widely as is merited. The pattern is never static but subject to endless changes from country to country and in different sections of the same country.

The devastating world-wide epidemics of the past happily seem to have disappeared, at least since that of the influenza epidemic during and following World War I. However, if this is the case, we should not be blinded to the possibility of newer, subtler, and more disastrous epidemics in view of the promise of biological or bacteriological warfare threatened in the future.

In the writer's medical school days the curriculum included instruction in the epidemics of cholera, yellow fever, plague, diphtheria, smallpox, meningitis—all of which occurred from time to time in this country. The older surgeons could recount experiences of what was known to them as "hospital gangrene," which would empty a hospital ward overnight. Other diseases of this type but of lesser proportion have had a decreasing incidence; for example, typhoid fever and diphtheria. Malaria, formerly a scourge in the Mississippi Valley, is now, fortunately, almost nonexistent except in rural areas; however, poliomyelitis is much more widespread, and neither tularemia nor Rocky Mountain spotted fever is confined to the locality of its origin.

Dermatophytosis, introduced into the United States following the Spanish-American War, is widespread, and though its dangers are few, if any, it causes great discomfort and is a nuisance, especially to radiotherapists. Future developments alone will tell what payment for diseases introduced into this country will be made as an aftermath of World War II.

How and in what manner do these general considerations concern radiological practice? Radiologists must have been aware for a long time of the diminishing number of particular diseases or conditions they encounter which were formerly commonplace. Having this in mind, it is believed that it is time to take stock of what has been done in the past in the radiological field. Having this in mind, it was believed that an analysis of the diseases and injuries in which roentgenography has proved its use over a long period would be useful, interesting, and of practical value.

The skeleton was chosen for this purpose, as it was the anatomical system in which roentgenology first established its worth and had earlier attained a higher degree of value than in the respiratory, gastrointestinal, or genitourinary systems.

How recently has any reader seen a tabetic gait in public? How often has he been requested to treat tuberculous lymphatic nodes with roentgen rays? How often does he see a spina ventosa or a saber shin? How has the use of the sulfa drugs and their later successors influenced his opinion in films of the paransal sinuses, mastoids, and suspected osteomyelitis? Lobar pneumonia and post-pneumonic empyema are happily rarely found. It is hoped that an analysis of this large material (Fig. 1) of bone conditions will show the following: the vast increase in the proficiency of the roentgenologist; the advance in technique and apparatus; an increased resort to roentgen examinations in disease and injuries to the skeleton, and metabolic diseases which affect the skeleton.

* From the Edward Mallinckrodt Institute of Radiology of the Washington University School of Medicine, St. Louis, Missouri. Presented at the Forty-Ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 14–17, 1948.

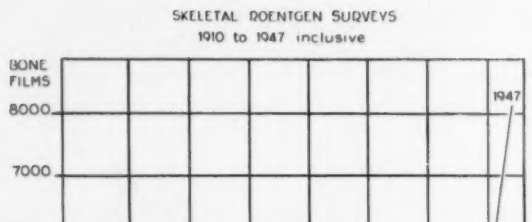


Fig. 1

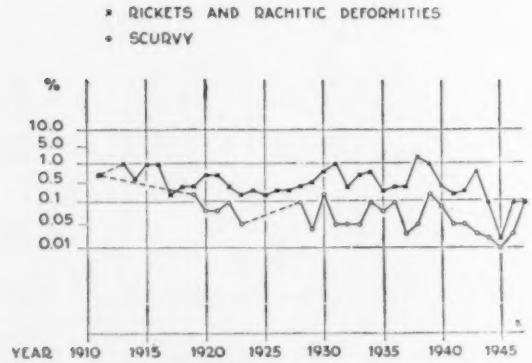


Fig. 2

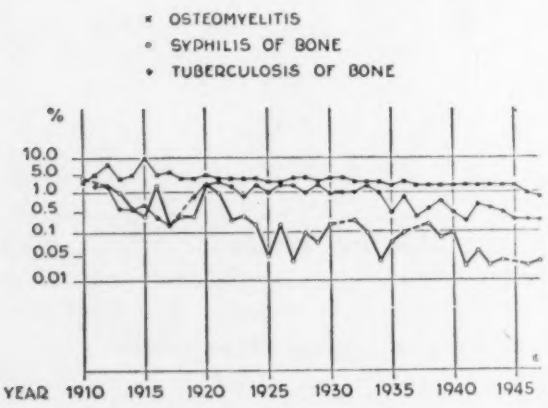


Fig. 3

In advance of collecting the data for this paper, there was a hope that the analysis would show a decreasing incidence of the worst types of disease of the skeleton (Fig. 2 and 3). It was also expected that fractures would show a change over the years traceable to the automobile, industrial accidents, etc. It will be seen later that this has not been entirely the case; while some of the worst diseases have lessened, others, such as metastatic carcinoma, have shown a rapid increase especially in the last few years.

Few readers have any knowledge of the limitations of equipment and roentgen-ray tubes at the early period at which these records begin. For this, the roentgenologist should be thankful. For example, satisfactory roentgen examination of the lumbar spine in the lateral projection was a brilliant (and accidental) achievement until Hollis Potter devised his diaphragm, which was not too long ago.

Undoubtedly, the 29 bone cases roentgenographed in 1910 represented a very active interest in and dependence on this type of examination. The percentage for the year 1947 will be given later. It should be of interest to roentgenologists that the x-ray department of the old Washington University Hospital was organized by the late Russell D. Carman.

The roentgen-ray records from 1910 to 1947, inclusive, are a composite representation of the opinions of many junior men, past and present. The many errors of inclusion should offset the number of errors of omission, since the number of cases included in this study is so large. I assume that I probably made more errors than any of the others in making these reports; in any event, the mistakes are mine.

Of the 87,899 individuals with examination of part or all of the skeleton, 55,245 were negative and 32,654 had a pathological condition of one kind or another. Naturally, some of the former were pathological and probably more of the pathological were normal or negative. Of the pathological cases the majority, as one would anticipate,

were fractures—21,677 (Fig. 4), and this includes both traumatic and pathological fractures even though the hospitals of the Washington University Medical Center have little traumatic surgery and the group includes such special hospitals as the St. Louis Maternity Hospital, where a fracture would be a rare occurrence.

The rarer diseases of bone were so few in number that they were not included in the percentages calculated by years. There were 24 cases of leontiasis ossea in the last thirty years; 8 cases of osteopetrosis in the last twenty-seven years, and over the same period, 18 cases of osteopsathyrosis; there were 2 examples of odontoma in twenty-five years; Kümmell's disease or deformity was seen 3 times in twenty years; osteopoicelia, 3 times in twenty-one years; sporotrichosis of bone, 4 times in the last eighteen years; 21 examples of xanthoma of bone in seventeen years; 15 adamantinomas in fifteen years; ivory vertebrae were observed 5 times in thirteen years; melorheostosis, 7 times in five years; symmetrical thinning of the parietal bone found twice in the last three years.

The reports on roentgenograms of the skull were intentionally omitted, as was meningioma, although fracture and osteomyelitis of the bones of the skull are included.

There were 164 cases of osteitis deformans including osteoporosis circumscripta (Fig. 5). There were 30 examples of osteitis fibrosa cystica. There were 73 cases of giant cell tumor which are not distributed by years. The joints have been omitted except neurogenic arthropathy and tuberculosis of the spine. Diaphyseal tuberculosis is rare, and in this material was found only in phalanges except in one case. Neurogenic arthropathy, naturally, comes under the heading of syphilis, though not included in the graph showing that disease (Fig. 6); and it, too, in the view of the writer, is chiefly but not entirely a disorder of bone, joint involvement being secondary, as is the case with tuberculous joints.

There is a large group of bone tumors in which the records did not state the type of tumor (Fig. 7). Among them were a number of metastatic tumors. In my opinion, metastatic tumors of the skeleton are prac-

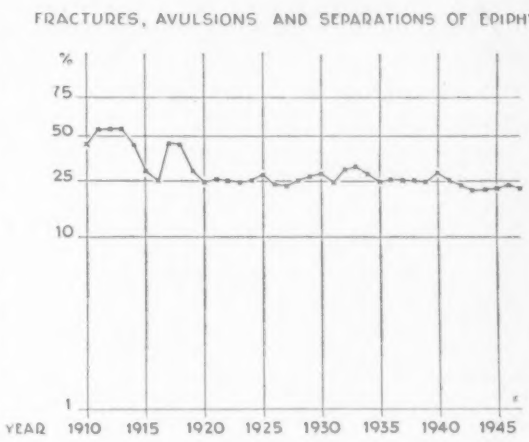


FIG. 4

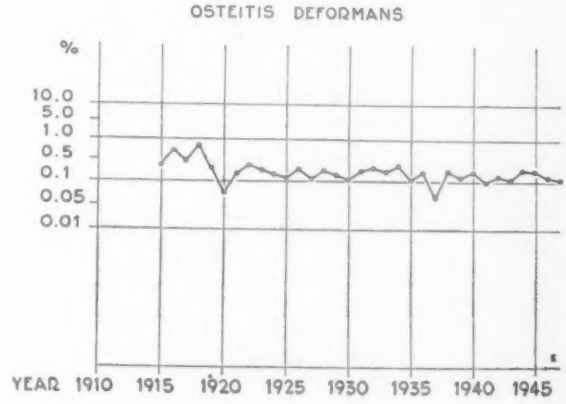


FIG. 5

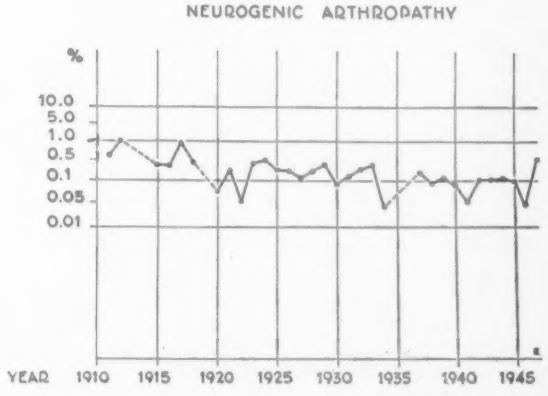


FIG. 6

tically exclusively of epithelial origin. The changing terminology applied to sarcoma of bone in the past four decades leaves recognition of this neoplasm still somewhat confused in the records. For the past two decades bone sarcoma has meant osteogenic

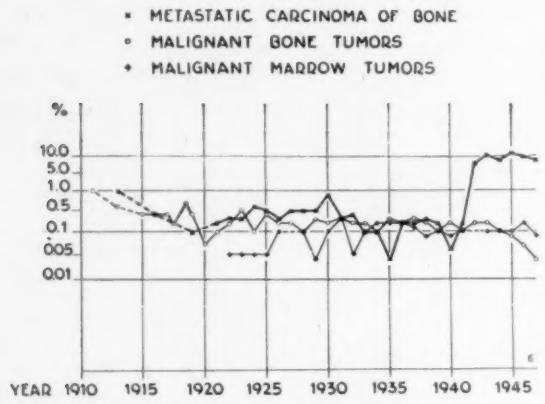


FIG. 7

sarcoma. The malignant diseases of the bone marrow are grouped together as myeloma, including the endothelial myeloma of Ewing (Fig. 8).

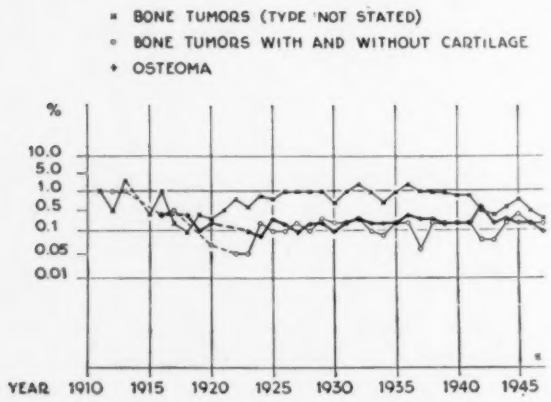


FIG. 8

That some of the cases of myeloma were actually sarcomas and that some of the sarcomas were myelomas is beyond question; but the greatest error would be found in mistaking myeloma for metastatic carcinoma of bone, or vice versa. However, the number is large enough that here, again, errors should cancel each other out.

There is a large number of reports of osteitis and periostitis with the type not given. In fact, they eluded more specific designation. The same is true of the number of cases of erosion of bone where the cause was not given—the cause not being stated because it could not be stated.

A digression is in order to point out that roentgenologic interpretation or opinion or report, whichever term one chooses to use, is, after all, but a memorandum opinion, and it is a lamentable fact that the radiologist gets confirmation or refutation of the opinion which he has expressed only with the greatest difficulty; indeed, the refutation is many times easier to secure than confirmation. The late Dr. R. W. Mills once put it this way: "It takes five minutes for a doctor to tell you that your x-ray diagnosis is wrong, and it takes three weeks of patient endeavor to find out if you were right."

In the calendar year 1947 there were 35,747 diagnostic roentgen examinations recorded here. The number of admissions to the hospitals of the Washington University Medical Center were 41,266. The figure for the number of roentgen examinations made on these hospital admissions is not available, but there were 9,850 ambulatory private patients who needed roentgen examinations. Of the total 35,747 roentgen examinations for the year, 8,110 were of the skeleton. This constitutes 22.4 per cent of the diagnostic procedures for the year.

## SUMMARY

The records of the cross-filing of roentgenograms from the years 1910 to 1947, inclusive, have been key-punched. By using the sorter, the records of 87,899 individuals, who had a skeletal examination in whole or part, were analyzed. Of the 32,654 with a pathological report, several interesting things were discovered; the most striking being the great increase in the roentgen examinations of the skeleton. Advances in roentgenological knowledge and practice are shown by the relatively recent record-

ing of the rarer diseases of bone. There is a marked decline in the incidence of syphilis and an almost equal decline in that of osteomyelitis. Bone tuberculosis has maintained a quite constant level since the year 1920. In traumatic conditions there was a marked decline in percentage in 1920 and since that year the curve has remained flat. Rickets and scurvy have shown a considerable decline with some upward peaks. Osteitis deformans and neurogenic arthropathy have a fairly constant percentage. Malignant bone marrow tumors were not recorded before 1922 and since 1926 have remained of fairly constant occurrence. There is a tremendous rise in metastatic carcinoma of bone since 1940; this could be accounted for by the more extensive investigations of patients with carcinoma and perhaps the greater longevity of such patients. At present metastatic carcinoma stands next to fractures in incidence. Malignant bone tumors are fairly constant. The relative incidence of bone lesions will vary according to the type of hospital. All in all, the analysis, though it contains many errors, nevertheless should be of interest to roentgenologists.*

510 S. Kingshighway Blvd.
St. Louis 10, Mo.

* For discussion, see page 386.

# THE ROENTGENOLOGIC EXAMINATION OF THE CERVICAL SPINE*

*By* JOSEPH C. BELL, M.D., *and* JAMES B. DOUGLAS, M.D.
LOUISVILLE, KENTUCKY

PAIN in the cervical area, the shoulder and arm has long constituted a major diagnostic and therapeutic problem. Knowledge of the causes of such pain has increased rapidly in recent years and definitive therapy, surgical or otherwise, has progressed. The causes of cervical and shoulder pain, as we all well know, are many. In some instances the pain is due to a lesion of the cord itself but these are uncommon. Much more frequent are lesions adjacent to the cervical cord with impingement upon the cord or the nerves leaving the cord. The latter are of many types, relatively common ones being rupture of the annulus fibrosus with extrusion of a portion of the affected disc into the spinal canal, hypertrophic arthritic changes that encroach upon the lateral foramina; primary and metastatic tumors and various traumatic lesions.

FIG. 1. Standard position No. 1. Lateral view of cervical spine. Normal.

The basic projections employed in our work are all standard and in no way original with us. Some such method of examination is employed by nearly all experienced roentgenologists but an outline of the plan of investigation we have found reliable and relatively simple may be of some value to the young roentgenologist who by trial and error or lack of knowledge of the methods of others has not as yet adopted a satisfactory procedure.

Position No. 1. (Fig. 1) The lateral projection. When possible the patient should be sitting or standing but when this is not feasible almost equally satisfactory roentgenograms can be secured with the patient supine, lying on a litter, the central ray being parallel to the top. A stationary grid is employed, the one described by Camp, with the grid a part of the cassette being used in our work but any other stationary one is satisfactory. The film size should be 10 by 12 inches. The lower margin of the cassette is placed approximately 1 inch below the level of the acromium and the roentgen-ray beam is centered at the level of the body of the fifth cervical vertebra. A 6 foot tube-film focal distance is employed. The neck is held in a neutral position and the patient required to fix her eyes on a point directly in front of her, respiration being suspended during the exposure. Films are made in flexion and extension when indicated but in our opinion do not yield sufficient additional information to justify their inclusion as a part of the basic examination.

* Presented at the Forty-Ninth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 14–17, 1948.

Position No. 2. (Fig. 2) Direct anteroposterior projection. An 8 by 10 inch film usually includes the upper two or three dorsal vertebrae, the surrounding area and all of the cervical spine with the usual exception of the first and second vertebrae. It is of value in detecting cervical ribs, lesions in the pulmonary apices such as primary bronchogenic carcinomas, subclavian aneurysms, substernal extensions of the thyroid and destructive lesions involving the lateral processes, many of which cause shoulder and arm pain.

Position No. 3. (Fig. 3) This projection is of the first and second cervical vertebrae made through the open mouth, the centering being immediately below a line that passes from the lower margins of the upper central incisors to the base of the mastoid. It is of particular value in demonstrating fractures of the odontoid, fractures of the arches of the first cervical vertebra and dislocations.

Fig. 2. Position No. 2. Direct anteroposterior view of cervical and upper dorsal spine. Cervical spine normal. Hemangioma of third dorsal vertebral body.

Fig. 3. Position No. 3. Visualization of first and second cervical vertebrae through open mouth. Normal.

Positions No. 4 and 5. (Fig. 4 and 5) These positions are the right and left posteroanterior oblique projections. They are of major value in demonstrating the lateral foramina, the lateral articulating processes, in demonstrating degenerative arthritic changes and in revealing hypertrophic deposits which may encroach upon the foramina and may, or may not, impinge upon the nerves passing through those in question. They are of value also in demonstrating many traumatic and other destructive lesions. In all instances where the normal anterior cervical curve is present the exposures are made with the patient prone, the head being placed in a true lateral position and the shoulder elevated so that the plane of the shoulders is at approximately 45 degrees to the horizontal. The centering is over the fourth cervical vertebra, the central beam being perpendicular to the film. The tube may be

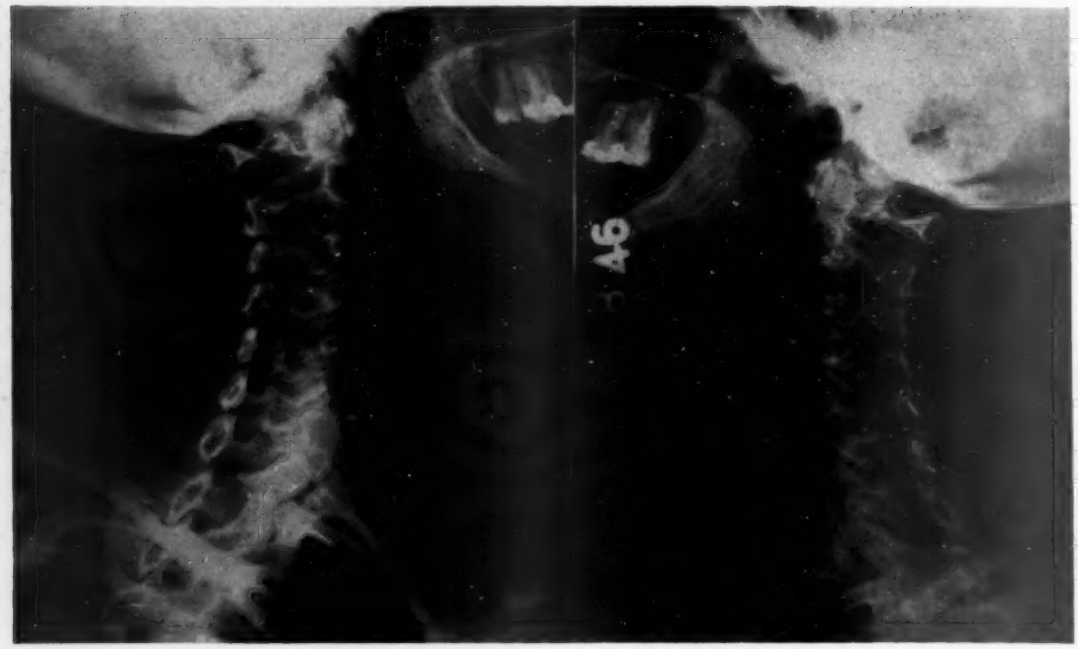

FIG. 4. Positions No. 4 and 5. Right and left posteroanterior oblique projections of cervical spine. Lateral foramina well shown. Normal. Lateral articulating processes also well demonstrated.

angulated somewhat toward the feet in individuals with large shoulders when the long axis of the cervical spine is not approximately parallel to the table top. In the presence of marked muscle spasm the anterior cervical curve may be absent and a reversal of the normal curvature present. In such instances the oblique projections are best made in the anteroposterior oblique positions rather than the posteroanterior as is usually true.

FIG. 5. Position No. 1. Lateral exposure of cervical spine. Fracture of dens with anterior displacement of dens and first cervical vertebra. Anterior dislocation of body of fifth cervical vertebra in relationship to sixth with fractures of posterior processes.

These are the five basic positions employed. We consider steresocopic views unnecessary except in special instances indicated by the preliminary findings.

### RUPTURE OF THE CERVICAL INTERVERTEBRAL DISC

Rupture of the annulus fibrosus with extrusion of a portion of the intervertebral disc into the spinal canal in the cervical region is now recognized as a relatively common clinical entity.

William B. Scoville of Hartford, Connecticut, at the meeting of the Harvey Cushing Society in San Francisco, August 20, 1948, reported an analysis of 68 operated cases, 22 of which had previously been reported, 12 by Spurling and Scoville and

10 by Whitcomb. The average age at the time of operation was forty-three years, the youngest being in the twenties and the oldest being in the fifties. There was a definite history of trauma in 50 per cent of the cases. The duration of symptoms was less than one year in 75 per cent of the reported cases and less than three months in 50 per cent. Pain was a symptom in all but one, numbness was present in 50 per cent and the spinal fluid protein was above 40 mg. per cent in 30 per cent of the cases and over 50 mg. in 20 per cent. In 42 cases analyzed in regard to the level of the herniation, 12 were found at the level of the fifth cervical interspace, 28 at the sixth and 2 at the seventh, the latter being the interspace between the bodies of the seventh cervical and first dorsal vertebrae. In 80 per cent the extruded material was soft in character and in 20 per cent hard, at times being partially calcified. Large defects were less common than small ones, those involving only the adjacent root sleeves. In 60 per cent of the cases localized proliferative arthritic changes were demonstrated in preliminary roentgenograms.

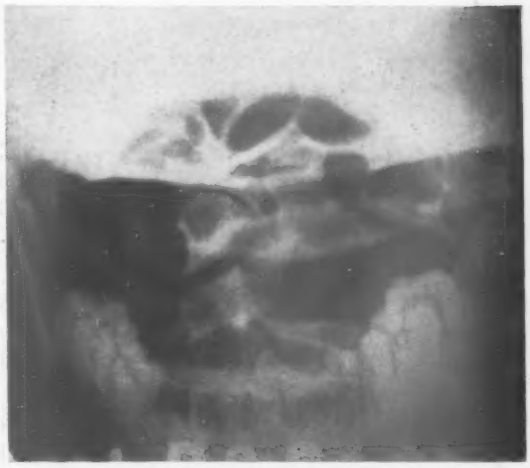

FIG. 6. Position No. 3. Fracture of dens with moderate angulation toward the right shown through open mouth.

Surgeons found quite early that some individuals having symptoms thought to be due to rupture of a cervical intervertebral disc showed no evidence of extrusion of any part of the intervertebral disc into

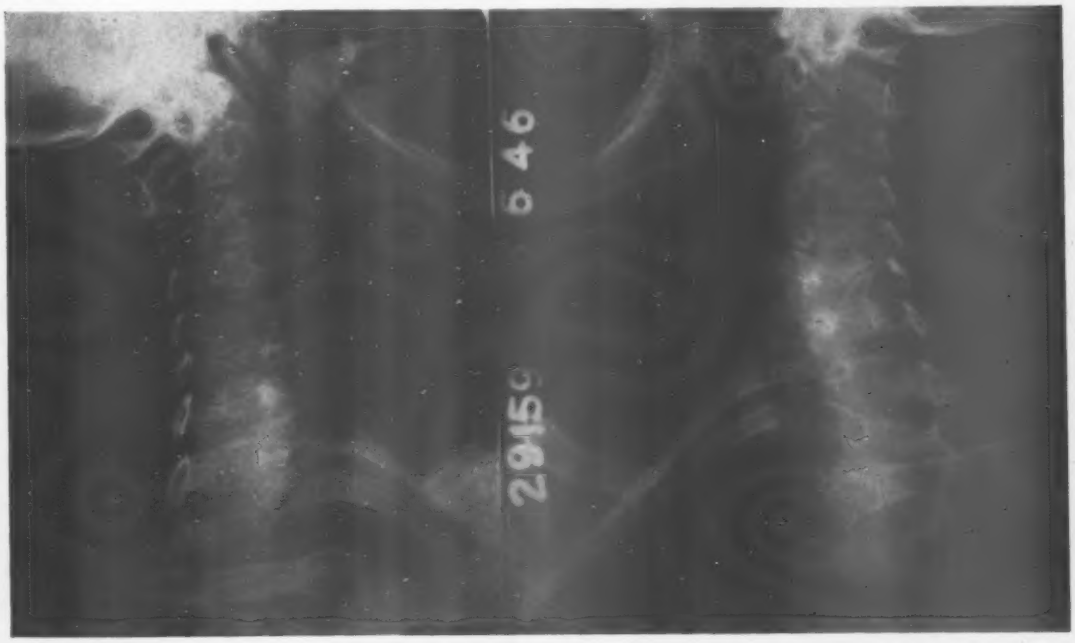


FIG. 7. Positions No. 4 and 5. Posteroanterior oblique views of cervical spine showing marked hypertrophic changes encroaching upon foramina between fifth and sixth and sixth and seventh cervical vertebrae on both sides.

FIG. 8. Cervical myelography. Normal. Axillary pouches well shown.

the spinal canal but instead showed hypertrophic changes that encroached upon a lateral foramen and in some instances quite obviously impinged upon the nerve passing through the foramen. It is because of the above and the many other cervical lesions that may produce symptoms simulating the presence of a so-called herniated nucleus pulposus that a very careful and complete roentgen examination of the cervical spine is essential.

### CERVICAL MYELOGRAPHY

Some neurologic surgeons believe the neurologic findings and history sufficiently definite, in many lesions of the cervical spine, to justify operation without myelography. Others continue to employ cervical myelography even in many instances where the clinical and neurologic findings are considered diagnostic.

After hearing the presentations and discussions at the Harvey Cushing Society in San Francisco, it is the impression of one of us (J.C.B.) that there now is a definite trend toward more frequent use of myelography in both the cervical and lumbar examinations, although during the previous

FIG. 9. Cervical myelography. Relatively large defect indicated by arrow at level of fifth cervical interspace at operation shown to be due to lateral rupture of annulus fibrosus with extrusion of a portion of the disc into the spinal canal.

two or three years the trend was in the opposite direction.

In our practice cervical myelography is always done in conjunction with a neurosurgeon and is always preceded by the above described standard roentgen examination of the cervical spine. Pantopaque is the contrast medium employed and much more accurate information is obtained when 6 cc. is injected instead of 3 cc. commonly used in myelography in the lumbar area. The patient is placed prone on the roentgenoscopic table, the head being at what is ordinarily the foot area in the event that a special two-way tilting table is not available. The latter is certainly in no way essential. The injection, in our examinations, is done by an experienced neurologic surgeon but in some other places may be done by an orthopedic surgeon or possibly some other physician especially trained in this particular work. Myelography, whether in the cervical or lumbar spine, however, should never be performed by one not thoroughly trained in the technique of the examination nor by one untrained in the neurologic manifestations of encroaching lesions in the spinal area.

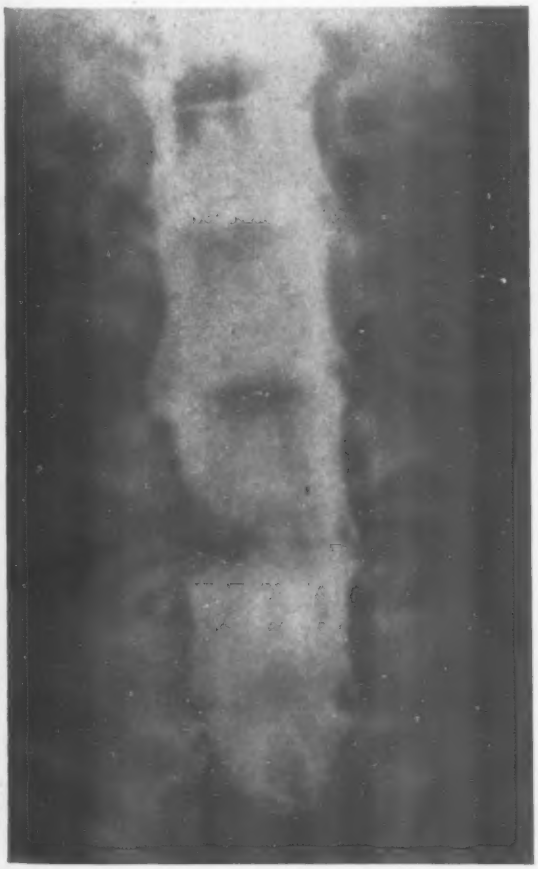

Fig. 10. Cervical myelography. Lateral defect indicated by arrow shown at operation to be the result of rupture of the corresponding intervertebral disc. Lesion at sixth cervical interspace.

Fig. 11. Cervical myelography. Very small defect with obliteration of axillary pouch at sixth cervical interspace indicated by arrow. At operation shown to be due to rupture of the intervertebral disc. The defect is small but very characteristic.

When the contrast material is passing from the lumbar region into the cervical area the chin should be elevated and the neck extended to the maximum degree, a position initiated by Spurling and Hampton

at the Walter Reed General Hospital during World War II. We have found it advisable to place the responsibility for the maintenance of the position on the one doing the injection.

After injecting the contrast material the table is tilted lowering the head and elevating the pelvis until the head of the column passes the point of greatest convexity in the dorsal region after which the patient is rapidly returned to the horizontal. From this point onward cervical myelography is as easily accomplished as is myelography in the lumbar area. The patient can usually be supported with no difficulty during tilting by having an assistant hold the lower extremities but in paralyzed individuals more adequate fixation is needed. Such a support is illustrated in *Radiology*, 1944, vol. *43*, page 437. It was designed by Frank H. Mayfield, M.D., of Cincinnati, Ohio, and in our hands has proved to be of great value.

In case a complete block is encountered it is wise to elevate the hips and lower the head to a point where there can be no question of the completeness of the obstruction. Complete blocks are relatively easy to demonstrate but are uncommon, partial obstruction being much more frequently seen. Serial exposure, with the column of contrast material at various levels throughout the cervicals and upper dorsal parts of the spinal canal, are always made whether or not defects are noted during the roentgenoscopic phase of the examination. This is essential for many lesions are small, often obliterating only the root sleeves and these rarely can be detected roentgenoscopically but usually are obvious in films. It is our usual practice to make the exposures through a narrow rectangular slit-like opening in the roentgenoscopic shutter using no grid, the exposure being controlled by a quick change-over switch. The films thus secured are of good diagnostic quality but contrast may be somewhat improved by the use of the moving grid in the table and since the column of contrast material can so easily be controlled there is no reason why this method of exposure is not entirely satisfactory. After the indicated films have been secured, when using the conventional table, it is necessary to reverse the position of the patient so that his head is at the head of the table and his feet rest against the foot support. The table is then tilted usually until the patient is almost vertical or until all of the contrast material returns to the lumbar area. He is then returned to the horizontal, the column of contrast material centered about the needle, the needle having remained in place throughout the examination, after which the pantopaque is removed by aspiration.

## CONCLUSIONS

1. An adequate standard method of roentgen examination of the cervical spine is essential. Such an examination should always precede myelography and is indicated in the large percentage of individuals presenting symptoms that might or might not originate in the cervical area.

2. Cervical myelography is neither time consuming nor difficult.

3. Accurate interpretation requires close cooperation between the roentgenologist and the neurologic surgeon or neurologist and demands a painstaking consideration of the history, the neurologic, roentgenologic and laboratory findings.

4. Those with whom we work believe cervical myelography yields information not obtainable by other means amply justifying its employment.

402 Heyburn Bldg.
Louisville 2, Kentucky

## DISCUSSION OF PAPERS OF MOORE, AND BELL AND DOUGLAS

DR. MAURICE M. POMERANZ, New York, N. Y. To one whose exclusive interest for the past generation has been orthopedic roentgenology, it is somewhat surprising as well as disappointing to see what casual interest is displayed by the average roentgenologist in this subject. Tangible evidence of this attitude is

the few papers on the program which are devoted to this subject.

Despite the fact that much has been said and a great deal written during the past decade regarding the mechanics and function of the skeletal system, very little is yet known regarding its specific role in many of the diseases which leave their imprint there.

It is for this reason that the studies of Doctors Bell and Moore are timely since they focus attention on a badly neglected field—that of orthopedic roentgenology.

Dr. Bell has divided his paper into three parts: a description of the technique for the examination of the cervical spine, a section dealing with the diagnostic significance of the presence of hypertrophic marginal spurs, and lastly myelography.

While techniques are recommended for the roentgenography of the cervical area, we routinely employ the usual anteroposterior and lateral views and occasionally the oblique views. In our experience these examinations are best performed with the patient in the erect position. We rarely employ the open mouth technique since we have found that the planigram is unexcelled for the demonstration of the first and second cervical vertebrae. Dr. Bell has rightly stressed that the impingement of marginal spurs on spinal foramina may account for some of the symptoms related to this area. This was emphasized almost twenty years ago by Dr. Lewis Gregory Cole. Our experience with cervical myelography has been limited. Curiously enough, however, we have encountered more tumors than herniated discs in this area. It is my feeling that we are too prone to relate symptoms to slight morphologic or structural changes in the cervical region, forgetting completely the complex soft tissues in this region which must unquestionably be responsible for some of the distress which we see.

I have not had the opportunity to read Dr. Moore's survey but the lantern slides which he has demonstrated yield a great deal of interesting information which cannot be reviewed in the few minutes allotted to me. It is my impression that it is hazardous to attempt to reconcile statistical experiences from one part of the country to another or, for that matter, from one hospital to another. These tables represent a review of what has occurred in a specific hospital in a specific locality. There are so many imponderables. Let me cite one example. If I were to attempt a statistical study of the incidence of congenital syphilis seen by me during the past twenty years at the Hospital for Joint Diseases, I would state that the disease is almost non-existent or at least extremely rare. Yet I am at the moment engaged in a study of 40 patients suffering from congenital syphilis and treated by penicillin at Bellevue Hospital. How would one reconcile these contradictory data for a statistical survey?

The great value of Dr. Moore's paper, to me at least, is the picture it gives of our success in conquering certain diseases. The problem of the increasing incidence of malignant bone tumors is one which we hope the present generation will solve.

It will be very profitable to read these two reports when they are published.

# BONE METASTASIS IN MALIGNANT MELANOMA*

*By* DANIEL WILNER, M.D., *and* ROBERT L. BRECKENRIDGE, M.D.
PHILADELPHIA, PENNSYLVANIA

THE important feature of malignant melanoma is its metastasis. The primary lesion may be small and insignificant, but its cells can secondarily invade and destroy any tissue including bone. It is the bone involvement, with its roentgen and pathological findings, that has created our interest in reviewing 83 cases of malignant melanoma.

To the best of our knowledge, only isolated articles have appeared in the literature describing the roentgen changes produced by osseous metastasis. One of these was a case described by Livingston[6] which presented an unusual manifestation of malignant melanoma developing in the lumbar region without evidence of a primary site in the skin or eye. Roentgen examination showed nearly complete destruction of the laminae, transverse and spinous processes of the second and third, with partial destruction of the body of the third, and beginning destruction in the body of the fourth and fifth lumbar vertebrae. Geschickter and Copeland,[4] in their series, had 3 cases with secondary deposits in bone. The lesions in the long bones were situated about the site of the nutrient vessels, showing marked destruction and expansion of the bone and some invasion of the soft parts. In one instance, a pathological fracture occurred in the middle third of the humerus. The bone lesions in the 6 cases described by Howes and Birnkrant[5] were uniformly lytic in character, round or oval in shape, having a clean, smooth edge without evidence of a cortical or periosteal reaction zone. The cortical bone was entirely resorbed within the bone. Only in one case was there an expansile lesion. Here, there was a mushrooming out of the head of the clavicle to about twice its normal diameter and with pathological fracture through its normal shell. Russo[8] reported 3 cases of malignant melanoma in infancy, 2 of which showed osteolytic lesions in bone. One case revealed symmetrical destructive lesions involving the lateral aspects of the distal metaphyses of both femurs, with little evidence of bone reaction. The second case presented similar areas of destruction in the vertebrae, left sacroiliac joint, both iliac bones and the upper ends of the femurs.

TABLE I

| Author | Cases | Bone Involvement | Per Cent |
|---|---|---|---|
| Geschickter and Copeland | 169 | 3 | 1.77 |
| Affleck | 317 | 9 | 2.84 |
| Howes and Birnkrant | 32 | 6 | 18.6 |
| de Cholnoky | 117 | 1 | 0.85 |
| Daland and Holmes | 174 | 12 | 6.89 |
| Moersch, Love and Kernohan | 97 | 2 | 2.06 |
| Our series | 83 | 9 | 10.84 |
| Total | 989 | 42 | 4.24 |

There is considerable variation in the incidence of osseous metastasis as reported by various authors. This incidence is tabulated in Table 1.

In our series of 83 cases of malignant melanoma, 9 showed evidence of bone metastasis. Of these, 45 had been studied by roentgen examination, 15 of which had complete bone surveys.

We are presenting 5 of the 9 cases, which show the bone involvement to best advantage.

## REPORT OF CASES

CASE 1. A twenty-five year old coal miner was sent to the hospital after a physician had incised an innocent looking tumor of the scalp

* From the Department of Radiology and the Clinical Laboratory of the Jefferson Medical College Hospital, Philadelphia, Pennsylvania.

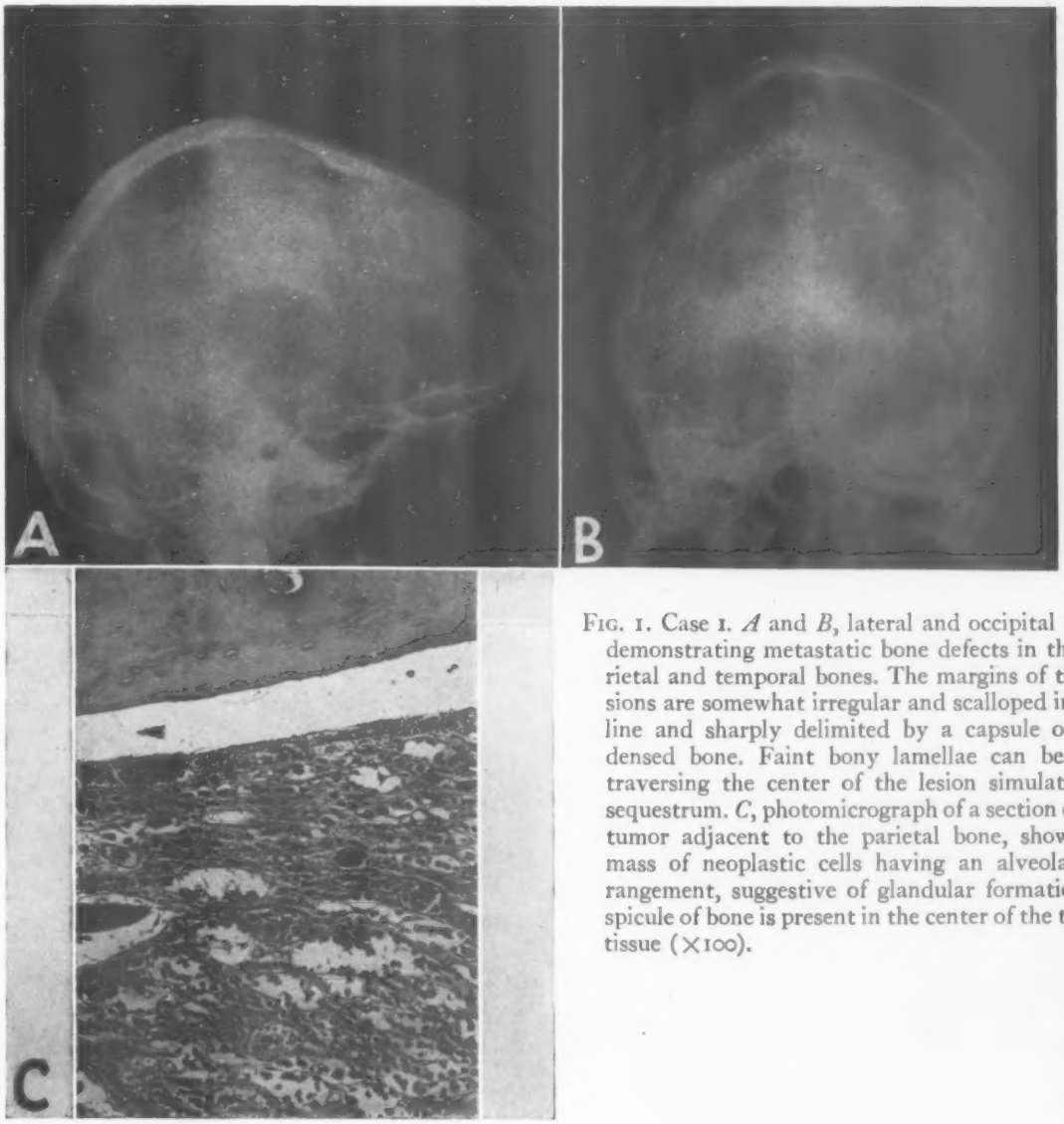


Fig. 1. Case 1. *A* and *B*, lateral and occipital views demonstrating metastatic bone defects in the parietal and temporal bones. The margins of the lesions are somewhat irregular and scalloped in outline and sharply delimited by a capsule of condensed bone. Faint bony lamellae can be seen traversing the center of the lesion simulating a sequestrum. *C*, photomicrograph of a section of the tumor adjacent to the parietal bone, showing a mass of neoplastic cells having an alveolar arrangement, suggestive of glandular formation. A spicule of bone is present in the center of the tumor tissue (×100).

and discovered, much to his surprise, that it extended into the calvarium. Two years prior to this, the patient had noticed a raised, dark red area below the right scapula, which bled profusely when traumatized, and subsequently he became aware of a mass in the right axilla about the size of a hen's egg. After an interval of one and a half years, the axillary mass began to increase in size and two firm, non-tender nodules appeared on the scalp. At this time he underwent a herniorrhaphy. While convalescing, the scalp nodules became tender, larger, and were accompanied by severe headaches. This was followed by fever, nausea, vomiting, soreness in the chest and pain in the back.

Examination revealed a well developed, well nourished young man with two subcutaneous nodules in the scalp, which were firm and fixed and measured 4 to 6 cm. in diameter. There was an internal strabismus of the left eye and papilledema of both discs of 2–3 diopters. A firm, non-tender, freely movable mass was felt in the right axilla measuring 8 by 4 by 4 cm., and a raised, red tumor, 2 cm. in diameter, surrounded by a margin of scar tissue, was observed 6 cm. below the right scapula. The erythrocyte count was 4.0 to 4.2 million per cu. mm. The sedimentation rate was 30 mm. in one hour. The urine did not contain melanin nor Bence-Jones protein. The glucose tolerance test

showed a diabetic curve. The patient's condition grew rapidly worse and showed signs of cerebral involvement. He died eighteen days after admission.

Roentgenographic examination of the skull disclosed metastatic bone defects which were represented by cyst-like translucencies in the parietal and temporal bones. The margins of the lesions were somewhat irregular and scalloped in outline and sharply delimited by a capsule of condensed bone. A smaller lesion, however, in the vault of the skull presented an oval cyst-like space with margins which were dense and smooth in configuration. Faint bony lamellae could be seen traversing the center of one of the cranial defects simulating a sequestrum. The remainder of the skeleton was negative for bone metastasis.

Necropsy revealed two firm tumors within the scalp, measuring 6 and 9 cm. respectively, and situated just to the left of the midline in the left temporal region. Both tumors involved the thickness of the scalp and the adjacent bone. The tumors were composed of fleshy, grayish-yellow, solid tissue. The defects in the bone penetrated both tables and were rather jagged in contour. A similar tumor was seen in the subcutaneous tissues of the right axilla measuring 7 cm. in diameter. A slightly raised, oval nodule, measuring 1 cm. in diameter, was present on the right side of the back, at the level of the tenth thoracic vertebra. The peritoneal cavity contained 75 cc. of a turbid, brown fluid. The stomach had four perforations ranging from 0.5 to 2.0 cm. in diameter, which were located on the posterior wall of the fundus. The microscopic diagnosis was malignant melanoma.

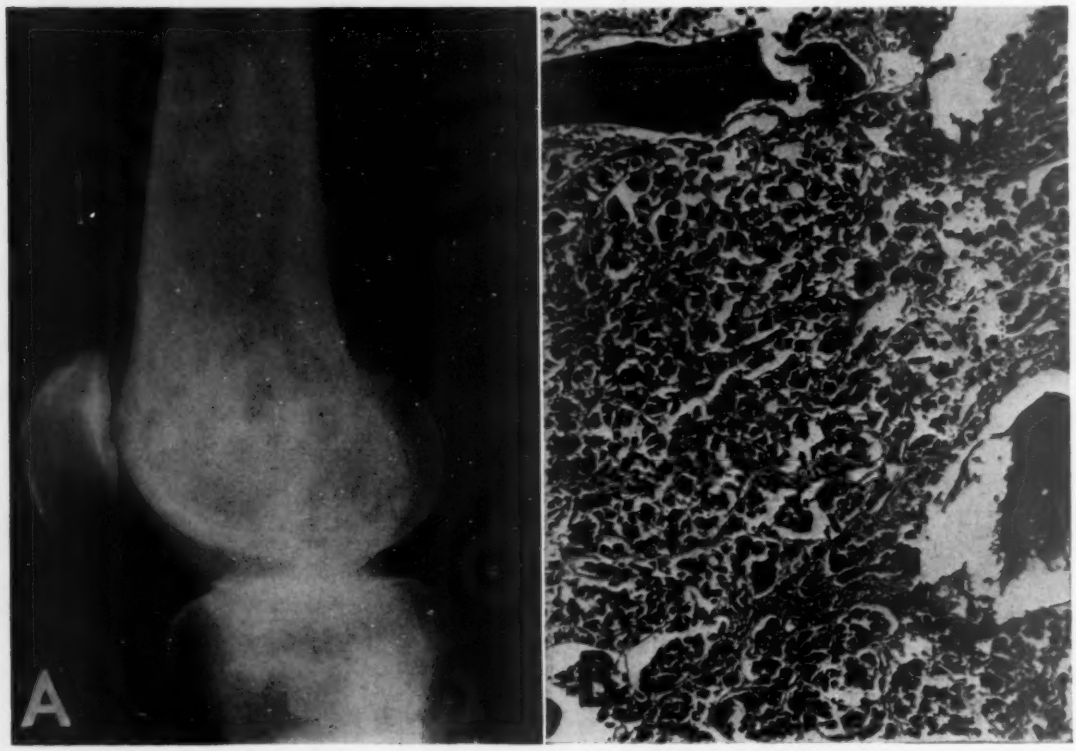


FIG. 2. Case II. *A*, showing a metastatic process in the distal shaft of the femur. The periosteum and cortex show an interruption in their normal contour and irregular fragments of bone can be seen projecting into a large soft tissue tumor. *B*, photomicrograph reveals several fragments of adult bone surrounded by heavily pigmented neoplastic cells (×100).

CASE II. A white man, aged sixty-seven, gave a history of having squeezed a pimple on his right cheek about two years before admission to the hospital, and then continued to irritate it while shaving. The lesion never healed completely but instead increased in size. One

month prior to admission, he noticed lumps appearing first on his left elbow and then over other areas of the body. He complained of generalized joint pains and stated that he lost 40 pounds (18 kg.) in weight. His past history revealed that a mixed tumor of the right parotid gland had been excised thirty years previously and that the left eye was enucleated following trauma.

Examination disclosed a poorly nourished, weak and ill looking man, with multiple subcutaneous nodules, an ulcerating tumor of the right cheek measuring 3 cm. in diameter and a swelling of the lower third of the right femur. The erythrocyte count was 2.65 to 2.80 million per cu. mm. He died one month after admission.

Roentgenographic examination revealed a metastatic process in the distal shaft of the femur characterized by an irregular area of rarefaction which gradually faded off into normal bone density. The periosteum and cortex showed an interruption in their normal contour and irregular fragments of bone could be seen projecting from the cortex into the adjacent soft tissues. There was considerable soft tissue swelling about the area of bone involvement.

Necropsy revealed a foul smelling, ulcerated, grayish-black tumor in the skin of the right cheek, measuring 2.5 by 1.0 cm. There were numerous subcutaneous nodules over the entire body varying from 0.3 to 5.0 cm. in diameter. They were sharply circumscribed, freely movable, grayish-black in color and firm in consistency. There were five tumor masses in the mucosa and the submucosa of the stomach, one in the duodenum, thirty-three in the small intestine and five in the large intestine. They were pedunculated or sessile in character and varied from 0.2 to 5.0 cm. in diameter. There were metastatic foci in the mesenteric, aortic and mediastinal lymph nodes, myocardium, peritoneum, pancreas, right kidney and suprarenal gland, brain, right clavicle and the lower end of the right femur.

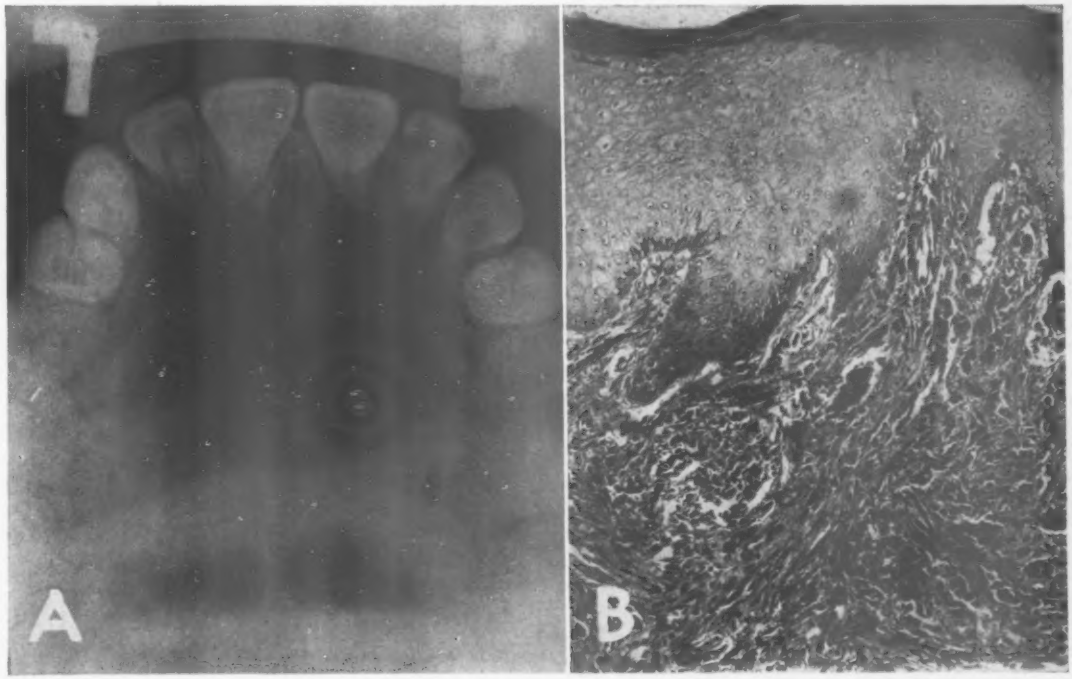


Fig. 3. Case III. *A*, showing an osteolytic lesion in the right maxilla. A few bony striae can be seen traversing a rather uniform area of translucency. *B*, photomicrograph showing the dermis and dermal papillae thickly invaded by large, darkly pigmented, spindle shaped cells. Clumps of these neoplastic cells are also seen in the capillaries and lymphatics (×100).

Case III. A female, Negro, aged thirty, complained of a painful growth on the roof of the mouth and swelling on both sides of the face.

About two months before admission to the hospital, she noticed a small lump on the roof of the mouth which rapidly increased in size. A month later, the sides of the face became swollen and painful. Examination disclosed a sessile, macerated, ulcerated, grayish-white lesion involving the entire hard palate and most of the soft palate with moderate induration of the surrounding tissue. The lymph nodes of the submaxillary and anterior cervical region bilaterally were enlarged, firm and tender. The erythrocyte count was 4.37 million per cu. mm. The leukocyte count was 15,600 per cu. mm. The Wassermann and Kahn reactions were negative. The patient was treated locally with radium and deep roentgen therapy to the chest. She died five months after her first visit to the tumor clinic. A necropsy was not obtained.

Roentgenographic examination revealed a rather uniform area of radiolucency in the right maxilla. A few bony striae could be seen traversing the area of bone destruction. The lesion was sharply delimited medially by the median palatine suture while laterally it faded off into normal bone density. The remainder of the bony skeleton was negative for metastasis.

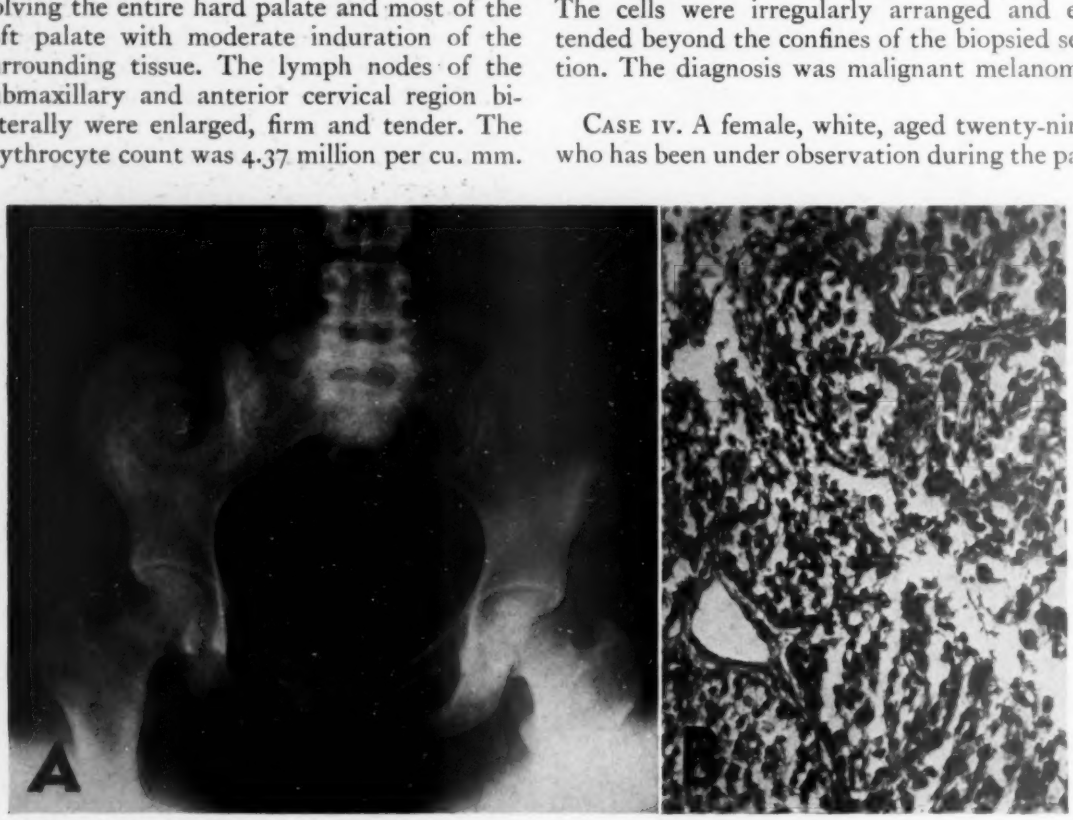


FIG. 4. Case IV. *A*, showing secondary metastasis in the right innominate bone. There are multiple areas of rarefaction interrupted by coarse bony spicules producing a "moth-eaten" type of bone destruction. The ragged and ill-defined contour indicates cortical involvement. *B*, photomicrograph of a lymph node biopsy, showing a replacement of the normal lymph node architecture by large masses of neoplastic cells. There are intracellular and extracellular deposits of dark brown pigment (×200).

Further roentgenograms revealed diffuse pulmonary metastasis.

A biopsy of the roof of the mouth revealed an invading tumor in the dermis composed mainly of irregular, large spindle-shaped cells that were heavily pigmented with dark brown pigment. The cells were irregularly arranged and extended beyond the confines of the biopsied section. The diagnosis was malignant melanoma.

CASE IV. A female, white, aged twenty-nine, who has been under observation during the past three years for metastatic malignant melanoma, began complaining of pain in her right hip. The patient stated that she first noticed a pinhead-sized growth on a toe of her right foot eleven years ago. Because the growth increased in size, she had it removed seven years later. At the time of removal, she was informed that the lesion was premalignant. One year later, the right femoral lymph nodes became enlarged to about 5–6 cm. in diameter. The leukocyte count was 12,800 per cu. mm. The enlarged femoral lymph nodes were excised and diagnosed as metastatic malignant melanoma. Roentgenograms of the chest and skull were

negative for metastasis. With the present complaint, a roentgen study of the right hip showed secondary metastasis to the right innominate bone. The external aspect of the right iliac bone showed multiple small areas of rarefaction interrupted by coarse spicules of bone producing a moth-eaten type of bone destruction. The metastatic process invaded the cortex as indicated by its ragged and ill-defined contour. There is no evidence of metastasis to other parts of the body.

Case v. A white female, aged thirty, was admitted to another hospital with the history that she had had a mole on her back since birth. Two months before admission to the hospital, however, she noticed the mole had increased in size and subsequently began to bleed and discharge pus. Physical examination disclosed a pigmented tumor about the size of a cherry, which was elevated, ulcerated and freely movable, and was situated posteriorly between the fourth and fifth ribs on the left side. Three small, pigmented moles were seen adjacent and inferior to the larger lesion. The entire area was widely and deeply excised.

The surgical specimen grossly consisted of three brown, raised moles measuring 0.5 cm., 0.3 cm., and 0.1 cm. in diameter, respectively. In addition, there was an elevated grayish-brown mole, which was 1 cm. in diameter and was surrounded by a dark grayish-brown discolored area of skin, which was approximately 1.4 cm. in diameter. The microscopic sections showed the large ulcerated lesion to be characteristic of a malignant melanoma whereas the three smaller tumors were diagnosed pigmented nevi. The patient was discharged from the hospital on August 8, 1947.

The patient was readmitted fourteen months later complaining of a "lump" at the site of the incision. Shortly thereafter, she noticed another "lump" under her right breast. Physical examination disclosed a firm, freely movable nodule, about the size of a grape, beneath the right breast. Another similar nodule was felt on the right chest, posteriorly, about the level of the angle of the scapula.

Roentgenographic examination of the left shoulder girdle revealed an osteolytic lesion at the external end of the clavicle. The involved segment of the clavicle showed a ragged type of bone destruction with expansion of the bone and pencil line thinning of the cortex along the inferior margin. The remainder of the bony skeleton was free of pathology. A roentgenogram of the chest showed two discrete nodular densities in the right second and third anterior interspaces in juxtaposition to the right hilum, denoting pulmonary metastases.

Fig. 5. Case v. *A*, showing an osteolytic lesion in the external end of the left clavicle, which is characterized by an irregular area of bone destruction with expansion of the bone and thinning of the cortex to a penciled outline along the inferior margin.

The patient was referred, at this time, to the tumor clinic of our hospital regarding further treatment.

## DISCUSSION

A review of the literature revealed only a few references regarding the subject of bone metastasis of malignant melanoma, although there are a number of papers dealing with metastasis elsewhere. A considerable number of cases, no doubt, go unrecognized simply because the majority of radiologists do not routinely take roentgenograms of all the bones of the body. At a necropsy it is likewise not practical to study the entire skeleton in great detail, particularly in the absence of a definitely known bone lesion. This would lead one to suspect that metastasis of malignant melanoma occurs more frequently to bone than is generally realized.

There is nothing characteristic about the roentgenological findings which might lead to a diagnosis of malignant melanoma. The cases in our series showing metastatic de-

posits in bone are all of the osteolytic type, but they show considerable variations in the nature of the lysis. Some of the bone lesions were cyst-like in character with dense margins of reactive bone, while the margins of other lesions were ill defined, gradually fading off into the normal bony architecture. Irregular bony lamellae were noted in several cases tending to produce a honeycomb appearance. In one instance a spotty, moth-eaten type of bone destruction was demonstrable. In several cases, the overlying cortex and periosteum were destroyed without evidence of periosteal new bone formation.

These lesions are not unlike those seen in other osteoclastic diseases such as metastatic carcinoma, lymphosarcoma, leukemia and Hodgkin's disease, while the lesions demonstrated in the skull may be mistaken for fibrous dysplasia or cholesteatoma (except that they are usually solitary lesions).

## CONCLUSIONS

1. Skeletal metastasis was investigated either by roentgen or necropsy examination in eighty-three patients with the diagnosis of malignant melanoma.

2. Of these eighty-three cases with malignant melanoma, nine cases, or 10.84 per cent, revealed skeletal metastasis.

3. Bone metastasis is more common than is generally realized. A more thorough bone survey by means of roentgen and necropsy examinations would undoubtedly uncover a greater number of cases.

4. The roentgenological findings are by no means specific for this disease.

5. The cases in our series showing metastatic deposits in bone are all of the osteolytic type, but vary considerably in the nature of the bone destruction.

The authors wish to extend their appreciation to Dr. James Surver, Clinical Director of the Department of Neoplastic Diseases, for his assistance in the preparation of this paper.

Jefferson Hospital
Philadelphia 7, Pa.

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# COLLAPSE OF THE VERTEBRAL BODIES IN SICKLE CELL ANEMIA*

*By* WILLIAM A. HENKIN, M.D.
NEW YORK, NEW YORK

THE reported osseous manifestations of sickle cell anemia have been many and varied.[2,3,5,12,14] Only rarely, however, has the occurrence of collapse of the vertebral bodies been noted.

Changes in the vertebral bodies were apparently first described in 1932 by Leivy and Schnabel[10] in their paper on abdominal crises in sickle cell anemia. Their Case 1 was a Negro male, aged twenty-five, hospitalized in October, 1926, because of severe pains in the arms and legs. The skull showed "considerable thickening of the outer table of the parietal bone. This was due to new bone formation, showing as striations perpendicular to the long axis of the skull." In the spine "the vertebrae were shortened in their vertical dimensions and somewhat widened in diameter. They had a soft appearance, there being considerable decalcification. The trabeculae were rather prominent and sharp and the cancellous spaces were rather large."

In 1937 Diggs, Pulliam and King[4] presented the most thorough discussion of the pathological and roentgenographic changes in sickle cell anemia. They noted that the vertebrae "show, as do the other cancellous bones, diffuse and localized variations in radiability. In addition there is, in adults with the disease, flattening of the vertebral bodies. . . . Average measurements of the height and width of the first four lumbar vertebral bodies in the anterior-posterior and lateral views revealed a greater height-to-width ratio in sickle cell anemia patients than in normal controls." The height-to-width ratios in 14 normal Negro adults was 1:1.4 in the anteroposterior view and 1:1.2 in the lateral view. In 7 patients with sickle cell anemia the mean height-to-width ratio was 1:1.9 in the anteroposterior view. For 8 other patients with sickle cell anemia the mean height-to-width ratio was 1:1.45 in the lateral view. There was no apparent relation between the age of the patient and the magnitude of the vertebral body changes.

The same vertebral body changes were observed by Weens[15] in 1945 incidental to a paper on cholelithiasis in sickle cell anemia. The roentgenographic report in his Case 1 stated that "the dorsal and lumbar vertebrae showed a rather coarse trabeculation and were somewhat osteoporotic. The vertebral bodies appear decreased in height and increased in width."

Kraft and Bertel[9] in 1947 reported a case of sickle cell anemia in a Negro male, aged forty-three. The following roentgenographic changes were noted in the spine: "Ballooning of cervical discs with biconcave shape of cervical bodies. Coarse trabeculation of vertebrae. Thinning of thoracic discs and exaggeration of thoracic curve. Flattening, lipping and coarse trabeculation of thoracic bodies with porotic areas posteriorly." In the lumbosacral spine, "lipping and flattening also sclerotic and porotic areas of vertebral bodies as seen in the thoracic area. Ballooning of discs as found in the cervical region. Exaggeration of the lumbosacral curve."

## CASE REPORTS

CASE 1. H. W., Negro, male, aged fourteen, was first admitted to Morrisania City Hospital on December 4, 1946, because of a draining left pretibial ulcer.

Since the age of three this boy had had innumerable attacks of muscle and joint pains, frequently accompanied by chills, fever, abdominal pain and jaundice, and occasionally by dyspnea on effort, palpitation and precordial pain. There had been no nausea or vomiting. At the age of three, his left leg was swollen. Thereafter, frequently after only moderate trauma, the skin over the anterior surface of the

* From the Department of Radiology, Morrisania City Hospital, New York, Dr. Samuel F. Weitzner, Director.

left tibia had broken down, draining seropurulent fluid for varying periods of time. Splenectomy was performed when the patient was four years of age. No change in the frequency or severity of the attacks was perceptible postoperatively.

Positive findings on physical examination of this thin but well developed Negro boy were slight icterus, small shotty axillary, epitrochlear and inguinal lymph nodes and a well healed scar of a left pararectus incision. There was pronounced anterior bowing of the left tibia with a yellow-crusted ulcer about 4 cm. in length overlying the anterior surface of the leg.

Fig. 1. Case 1. Left tibia, demonstrating anterior bowing, coarse trabeculation and cortical thickening. These changes bear a striking resemblance to those seen in Paget's disease.

Examination of the blood disclosed a red blood cell count of 2,400,000 with a hemoglobin of 58 per cent and a white blood cell count of 9,250, with 39 per cent neutrophils, 52 per cent lymphocytes, 8 per cent eosinophils and 1 per cent basophils. On direct smear marked anisocytosis and poikilocytosis as well as sickling were noted. There was 90 per cent sickling on a twenty-four hour wet preparation. Urinalysis was negative as was the blood Kahn test. Blood chemistry studies revealed a normal blood sugar and urea nitrogen, an icterus index of 17 with the qualitative Van den Bergh direct-negative, indirect-positive.

Roentgenograms of the skull showed no abnormalities. The long bones were all normal with the exception of the left tibia (Fig. 1) which showed considerable anterior bowing, coarsening of the trabecular structure and cortical thickening.

Fig. 2. Case 1. Dorsolumbar spine.

During his hospital stay he complained of muscle and bone pains in both upper and lower extremities. A low grade temperature ranging as high as 100.2° F. gradually returned to normal. Symptomatic therapy, two 500 cc. blood transfusions and wet dressings to the draining pretibial ulcer produced marked improvement. Pains abated, hemoglobin rose to 75 per cent, the draining ulcer healed and the patient was discharged on December 21, 1946.

He remained well until June 9, 1947, when he developed pain in the lumbosacral region and fever.

On admission to the hospital jaundice was not observed. The temperature was 100.8° F. The previously noted left pretibial ulcer was healed. There were no other significant findings.

Examination of the blood disclosed a red blood cell count of 3,490,000 with 11 grams of hemoglobin and a white blood cell count of 12,900, with 70 per cent neutrophils, 22 per cent lymphocytes and 8 per cent monocytes. Poikilocytosis and sickling were noted on direct smear with 70 per cent sickling seen on a twenty-four hour wet preparation. The icterus index was 18, the serum calcium 11.3 mg. per 100 cc., the serum phosphorus 3.6 mg. per 100 cc., the serum alkaline phosphatase 7.8 King-Armstrong units. A qualitative Sulkowitsch test revealed increased urinary calcium excretion.

On July 14, five weeks after admission the red blood cell count was 2,780,000 with 8.5 grams of hemoglobin and a white blood cell count of 11,400, with 43 per cent neutrophils, 50 per cent lymphocytes and 7 per cent eosinophils. Seven per cent reticulocytes were noted as well as sickling on direct smear.

Fever and pains gradually disappeared and the patient was discharged. Six weeks after discharge a repeated serum calcium determination was 11.1 mg. per 100 cc. and an alkaline phosphatase determination was 12.8 King-Armstrong units.

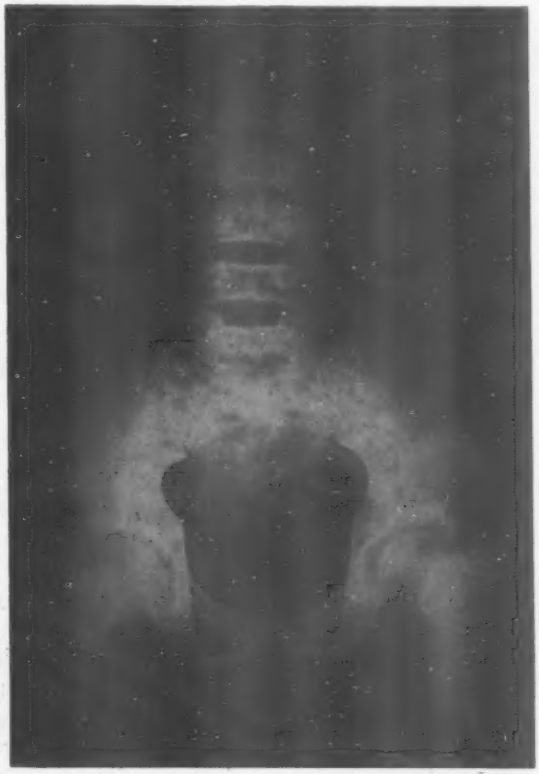

Fig. 3. Case 1. Lumbar spine and pelvis.

Fig. 4. Case 1. Lumbar spine, lateral view, showing collapse of the vertebral bodies with coarsening of the trabular structure and ballooning of the intervertebral discs.

Roentgenographic studies, during this admission, of the spine and pelvis were of unusual interest (Fig. 2, 3 and 4). The bodies of all the thoracic and lumber vertebrae showed coarsened trabecular structure with considerable diminution in height. This flattening of the vertebral bodies was accompanied by ballooning of the intervertebral discs. The cervical spine showed no abnormalities. Averaged measurements of the involved vertebrae, as suggested by Diggs, Pulliam and King,[4] gave the following ratios (Table 1):

Table I

HEIGHT-WIDTH RATIOS—CASE 1

| | Antero-posterior View | Lateral View |
|---|---|---|
| Thoracic vertebrae | 1:2.3 | 1:1.7 |
| Lumbar vertebrae | 1:1.8 | 1:1.7 |

Case II. J. C., female, Negro, aged twelve and a half, was admitted to Morrisania City Hospital for the sixteenth time on December 4, 1947, because of the sudden onset of pain in the left knee.

At the age of three she was admitted to another hospital because of anorexia and pain in the back and legs. On physical examination shotty, generalized lymphadenopathy was observed. The spleen was palpable 3 cm. below the costal margin; the liver, 1 cm. below the costal margin. A blowing systolic murmur, maximal at the apex, was audible over the entire precordium and was transmitted to the left axilla.

Fig. 5. Case II. Lateral lumbar spine shows ballooning of the intervertebral discs and slight central compression of the vertebral bodies.

Examination of the blood disclosed a red blood cell count of 2,580,000 with a hemoglobin of 40 per cent and a white blood cell count of 13,000, with 30 per cent adult neutrophils, 8 per cent juveniles, 4 per cent metamyelocytes, 58 per cent lymphocytes and 24 per cent nucleated red cells. There were 200,000 platelets. On direct smear anisocytosis, poikilocytosis and a few sickle cells were noted. A twenty-four hour wet preparation showed 95 per cent sickling. A fragility test showed no hemolysis 0.72–0.44 and partial hemolysis 0.40–0.24. Examination of the bone marrow revealed a hyperplastic, erythroblastic bone marrow with the most bizarre nuclear degeneration.

Fig. 6. Case II.

Roentgenograms of the skull and long bones showed no abnormalities. Mantoux test, Wassermann reaction and urinalysis were negative.

Under treatment with iron the hemoglobin rose to 52 per cent and the red blood cell count to 3,630,000. The spleen became somewhat smaller and the patient was discharged two weeks after admission with the diagnosis of sickle cell anemia.

Subsequently she was admitted to Morrisania City Hospital on sixteen occasions. Three admissions were for lower lobe lobar pneumonias confirmed by roentgenograms and responding well to chemotherapy. The remainder were for abdominal pain, pain in various joints, low back pain, or transfusion. A low grade fever, red blood cell counts ranging between 2,000,000 and 3,600,000, icterus indices varying from 12 to 27 and normal roentgen studies characterized these admissions, the diagnosis in each case being sickle cell anemia in crisis.

Symptoms and findings on December 4, 1947, were similar to those on previous admissions. However, roentgenograms of the lumbar spine showed slight coarsening of the trabecular structure and broadening of the lumbar vertebral bodies. There was no appreciable diminution in height except centrally where there was considerable ballooning of the intervertebral discs (Fig. 5 and 6).

## DISCUSSION

The following is the probable pathological basis for the roentgenographic changes in the vertebral bodies. Bone marrow examined both at autopsy and after bone biopsy is generally dark red in color and jelly-like in consistency. Microscopically great cellularity and congestion are noted. As in other organs of the body, congestion is frequently followed by thrombosis, infarction and connective tissue replacement of parenchyma. Sections may show, in addition, hemorrhage, granular and crystalline pigment deposits, hyalinization and abnormal calcification.[4] The resultant weakened bone, subject to excessive stresses, may show a tendency toward compensatory new bone formation.

It would appear, therefore, that two processes—trabecular destruction with connective tissue replacement, and new bone formation in the remaining trabeculae—develop simultaneously. The former produces gradual bone resorption manifested roentgenographically by a decrease in the number of bone trabeculae and by a general decrease in density of the affected bone. The latter produces an increase in the size of the remaining trabeculae, manifested roentgenographically by a coarsening of the trabecular structure and by a general increase in density of the affected bone. These changes occur primarily in the most erythropoietic portions of the bony skeleton, cancellous bone.

The connective tissue replacement of bony trabeculae is associated with a numerical decrease in osteoblasts rather than with any decrease in activity of the osteoblasts that remain. When the net result is that the osteoblasts do not lay down sufficient osseous matrix, the bone changes may be regarded as basically those of osteoporosis. "Since osteoporosis is not really a disease of calcium metabolism it is not surprising that the serum calcium and phosphorus levels are normal."[1] The serum alkaline phosphatase level, a measure of osteoblastic activity, is also within normal limits in osteoporosis.

In the vertebral bodies which are subject to the greatest mechanical stresses the coarsened trabeculae may prove incapable of giving adequate strength to the osteoporotic bone. A gradual collapse of the weakened vertebral bodies ensues. All the lumbar, most of the thoracic and, occasionally, some of the cervical vertebral bodies are involved. The extent of the changes is directly proportional to the duration of the disease, the severity of the anemia, and the body weight. It is for these reasons that the reported cases are in adults rather than in children.

The collapse occurs more or less simultaneously in all the affected vertebral bodies. It may be accompanied by mild or moderately severe, transient, self-limited, frequently recurring, poorly localized back pain.

The collapsed vertebral bodies show increased coarseness of the trabecular structure with coarse striations running superiorly-inferiorly. The bone density is as great as or perhaps greater than that of normal bone. As the intervertebral discs expand into the collapsing vertebral bodies, the latter assume a biconcave shape, the so-called "fish vertebrae."

The process differs only slightly from

senile osteoporotic collapse of the vertebral bodies[11] which is preceded by generalized bone atrophy and decalcification unaccompanied by coarsening of the trabecular structure. Senile collapse is often complicated by true pathological compression fractures of the vertebral bodies, an as yet undescribed occurrence in sickle cell anemia.

No similar changes in the vertebral bodies have been described in either Cooley's anemia or congenital hemolytic anemia despite the basic pathological similarity of the three diseases.

There appears to be a thought-provoking similarity between the osseous changes occurring in sickle cell anemia and those occurring in Paget's disease. The latter have been described[1] as developing in three stages: (*a*) destruction of bone due to an unknown cause; (*b*) osteoblastic stimulation due to increased stresses and strains; (*c*) overgrowth of bone and increase of the serum phosphatase level as a result of osteoblastic stimulation. "The original observation of Paget that the bone in osteitis deformans is hyperemic is certainly correct."[13] (The bone marrow hyperemia found consistently in sickle cell anemia should be recalled.) Skin temperatures are consistently and significantly higher over a portion of an extremity showing Paget's disease than over the corresponding portion of the opposite normal extremity. In Paget's disease the serum calcium and inorganic phosphorus levels are almost invariably normal. The alkaline serum phosphatase is elevated in proportion to the extent of osteoblastic bone involvement. In osteoporosis circumscripta of the skull, which appears to be a form of, or a stage in the development of, Paget's disease,[8] only the first stage of Paget's disease, destruction of bone due to an unknown cause, is present. The serum phosphatase is normal and there is hypofunction of the osteoblasts in the involved area. Roentgenographic examination of the lumbar vertebrae often shows vertebral body flattening very similar to that seen in sickle cell anemia except that the trabecular structure is much coarser. Depending upon the degree of coincident osteoporosis, ballooning of the adjacent discs may accompany the vertebral body flattening.

Another disease in which bone changes in the vertebral bodies should be expected is polycythemia vera. The bone marrow is extremely hyperplastic. Thromboses and hemorrhages are common complications. Yet a complete review of the literature has unearthed only one case[6] in which a relation between bone changes and polycythemia was noted. The patient was a white male, aged fifty-five, with a history of known polycythemia of thirty-one years' duration. At autopsy "in the bodies of the lumbar vertebrae the tan-red marrow was reduced to approximately one fifth of the usual volume. The bone trabeculae in the vertebrae were markedly thickened and the dimensions of the marrow spaces were correspondingly reduced. Along the edges of the trabeculae were narrow layers of newly deposited bone." Hirsch concluded that "the generalized osteosclerosis noted in the bones of this patient with polycythemia vera probably is a change occurring in the advanced chronic stages of the disease."

In 1946 Hodgson, Good and Hall[7] analyzed roentgenograms of 88 proved cases of polycythemia vera without finding any bone lesions attributable to the disease.

## SUMMARY

Two cases of sickle cell anemia, one in a Negro boy, aged fourteen, with osteoporotic collapse of the thoracic and lumbar vertebral bodies and the other in a Negro girl, aged twelve and a half, with similar changes in the lumbar vertebral bodies are presented. This is believed to be the first report of this finding in children.

In sickle cell anemia hemolysis of abnormal erythrocytes is followed by an intense erythropoietic reaction in the bone marrow with congestion, infarction and connective tissue replacement of cancellous bone. Coarsening of the trabecular structure is evidence of osteoblastic reaction in the weakened bone. The thoracic and

lumbar vertebral bodies, composed of cancellous bone and subject to great stresses, may show a gradual reduction in height.

Similar changes occur in Paget's disease (osteitis deformans). In senile osteoporotic collapse of the vertebral bodies there is no roentgenographic evidence of osteoblastic activity. Polycythemia vera, a disease in which hemorrhage and thrombosis are common complications, shows no bone changes similar to those found in sickle cell anemia; nor are such changes seen in Cooley's anemia or congenital hemolytic anemia.

20 Plaza St.
Brooklyn 17, N. Y.

ADDENDUM

Since submission of this manuscript two excellent relevant papers have appeared: LeGant, O., and Ball, R. P. Sickle-cell anemia in adults; roentgenographic findings. *Radiology*, 1949, *51*, 665–675; and Macht, S. H., and Roman, P. W. The radiologic changes in sickle-cell anemia. *Radiology*, 1949, *51*, 697–707. The former describes 4 cases, aged twenty-five, twenty-six, thirty-two, and sixteen, with similar changes in the vertebral bodies; the latter also records 4 such cases but does not state the patients' ages.

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# EVALUATION OF PLANIGRAMS IN PULMONARY TUBERCULOSIS*

*By* PHILIP MORGENSTERN, M.D., F.A.C.P., CHARLES E. CARR, M.D., *and* WALTER L. NALLS, M.D., F.A.C.P.

ALTHOUGH the introduction of antibiotics has raised the hope of eventually eliminating pulmonary tuberculosis by a single potent therapeutic agent, closure of cavities still remains one of the cornerstones in our present-day program of treatment. Any method of examination which helps to diagnose cavities more accurately is of considerable value.

Body section roentgenography is such a method. Although it has been in use under various names (planigraphy, laminagraphy, tomography, etc.) for almost twenty years,[1,4,5,6] it is still looked upon with skepticism by many roentgenologists and chest physicians. This attitude is due largely to the fact that there are many confusing shadows on the planigrams which are not seen on the conventional film. Unless a serious attempt is made to correlate these shadows with the actual lung findings, correct interpretation may prove very difficult.

Very few articles in the English literature deal with this phase of the subject. Epstein and his coworkers[2] in 1940 examined 10 cadavers shortly after death by means of tomograms and then compared the roentgen shadows with the lung findings at necropsy. They called attention to several pitfalls in the diagnosis of cavitation.

Our study attempted to check the accuracy of the planigraphic interpretations by correlating them with the sputum findings as well as with the actual lung findings in those cases which were treated by pulmonary resection. Three hundred consecutive sets of planigrams were reviewed. Twenty-three patients had had either lobectomy or pneumonectomy one to seven weeks after the planigrams were made and the interpretation could be checked with the actual lung specimen. The others were followed by careful check of the sputum and clinical course for periods of from five or six months to two years after the planigrams were made. This method, of course, is not as accurate as the correlation with resected lung specimens. With rare exceptions, however, it is justifiable to assume that a true tuberculous cavity will sooner or later give a positive sputum for tubercle bacilli. The presence of an annular shadow on a planigram with persistently negative sputum for six months or a year indicates that the suspicious density is probably not a cavity. Roentgenoscopy was also used liberally to check on the identity of suspicious oval or annular densities where diagnosis was still in doubt.

Using this approach, we came to certain definite conclusions:

A. Rigid criteria must be used in the diagnosis of cavity on planigrams:

1. There must be a complete, sharply defined, oval or annular density surrounding an area of increased radiolucence, usually showing on two or more roentgenograms at consecutive levels.

2. The walls of the suspected cavity must be clearly identified apart from adjacent structures such as pleura, rib, pulmonary vessel, or fibrous strand.

3. The suspected cavity should correspond in location with the site of the original cavity in cases where collapse therapy has been done.

4. In the case of a large radiolucent area within a dense post-thoracoplasty lung, identification of a bronchus leading into or stopping just short of the suspicious "high-

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light" is helpful in diagnosis of cavity. However, it was clearly seen in only 5 per cent of our cases.

B. Planigrams are most helpful in certain types of cases. These include:

1. Dense post-thoracoplasty lungs—the planigram is much more conclusive than a roentgenogram taken using the Potter-Bucky grid.

2. Extrapleural lucite pack—residual cavity may be obscured by the lucite balls on the conventional or Potter-Bucky film, but will usually be clearly demonstrated on planigram.

3. Inspissated cavity—this will show only as a uniform round or oval density on a plain roentgenogram but planigrams may reveal the central rarefaction within the caseous mass.

4. Dense fibrocaseous lesions.

Planigrams are of limited value in the following types of disease:

1. Confluent nodular densities scattered throughout the lung in several planes. These represent areas of caseation which may have tiny ulcerations too small to be demonstrated on planigrams taken at levels 1 centimeter apart. Such cavities are usually characterized by varying periods of negative sputum interrupted by an occasional positive concentrate or culture. It is very rare for such a cavity to give a persistently positive sputum on plain smear.

2. Planigrams may fail to demonstrate a slit-like cavity with collapsed walls in a thoracoplasty lung. Some air must be present within a cavity in order to produce the characteristic radiolucent area.

3. Emphysematous blebs and bronchiectatic dilatations within a fibrotic upper lobe may be very difficult to distinguish from small tuberculous cavities.[3,7] As a rule, however, emphysematous blebs tend to be more perfectly round and have thinner walls than tuberculous cavities. The extreme apical portion of the lung just beneath the pleura is a favorite site for emphysematous blebs.

In not a single case was a cavity discovered on the planigram in an area where no infiltration was seen on the plain chest roentgenogram. It is therefore useless to take planigrams of a lung which appears normal on the conventional roentgenogram.

The following cases illustrate some of the points mentioned above.

## CASE REPORTS

Case 1. E. C. B., a male, aged thirty, with a history of pulmonary tuberculosis since 1943. He had a six-rib thoracoplasty for cavitation in the left upper lobe. The sputum remained positive. Conventional roentgenogram showed moderate compression of the left upper lobe with a large ill defined highlight partly obscured by the thick overlying pleura. The Potter-Bucky roentgenogram was suggestive but not conclusive of cavitation (Fig. 1*A*). The planigram, however, showed a clearly demarcated 4 by 2 cm. cavity seen best on the 7 and 8 cm. levels, with two small bronchi leading to the lower border of the cavity (Fig. 1*B*). Cavernostomy was completed May 5, 1947, and the patient's sputum has been negative since July 22, 1947.

Case 11. A. P., a male, aged fifty-one. An extrapleural lucite pack operation was done on February 7, 1947, for a small cavity in the right upper lobe. Sputum, however, remained positive. On the plain film details of the compressed right upper lobe were obscured by the lucite balls (Fig. 2*A*), but the planigrams on March 25, 1947 and June 26, 1947 clearly showed the thick-walled residual cavity medial to the lucite pack (Fig. 2*B*). It was seen best on the 10 and 11 cm. films showing that it had been displaced far anteriorly by the lucite pack.

Case 111. B. D. M., a diabetic, aged thirty, who had pneumothorax on the left side for a tuberculous cavity in the upper lobe. Collapse was adequate and the roentgenogram showed a large caseous area at the site of the original cavity (Fig. 3*A*). Planigrams, however, showed a well demarcated, kidney-shaped area of radiolucence within the caseous mass, seen clearly on the 4, 5, and 6 cm. levels (Fig. 3*B*). Left upper lobectomy was done four weeks following planigrams and showed a partially inspissated cavity consisting of a hard cheesy periphery with a soft center containing greenish pus.

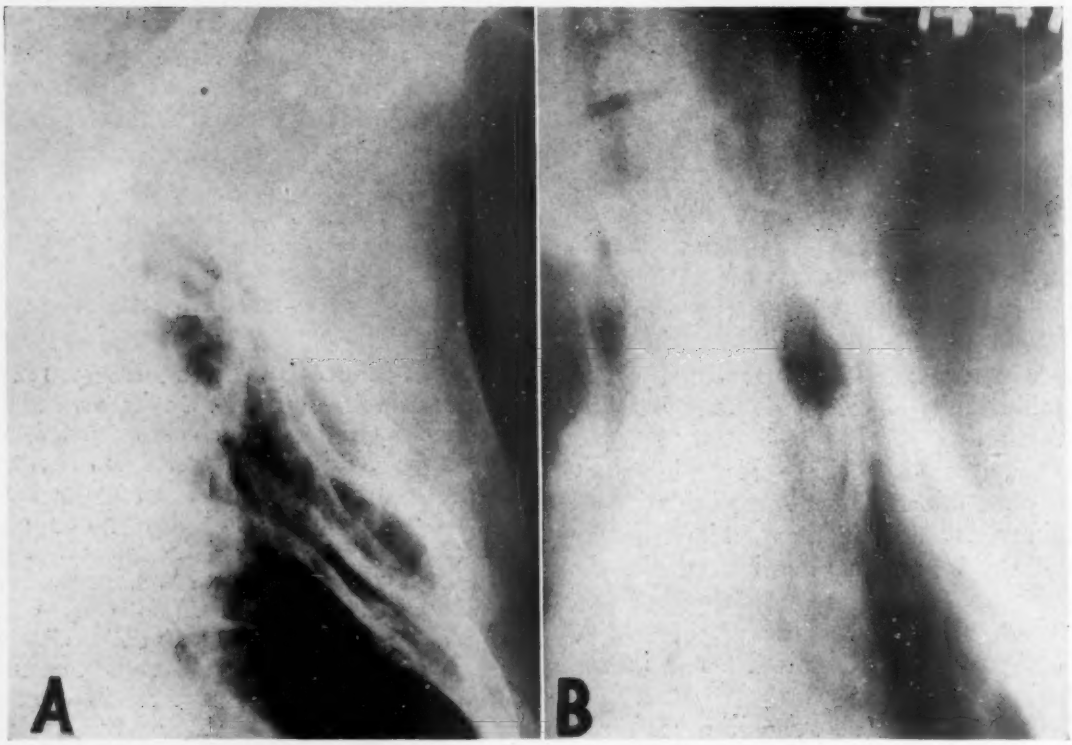


FIG. 1. Case I. *A*, Bucky film is merely suspicious of residual cavity in dense left upper lobe. *B*, planigram leaves no doubt about the presence of cavity. Bronchi are seen leading to the lower pole of the cavity.

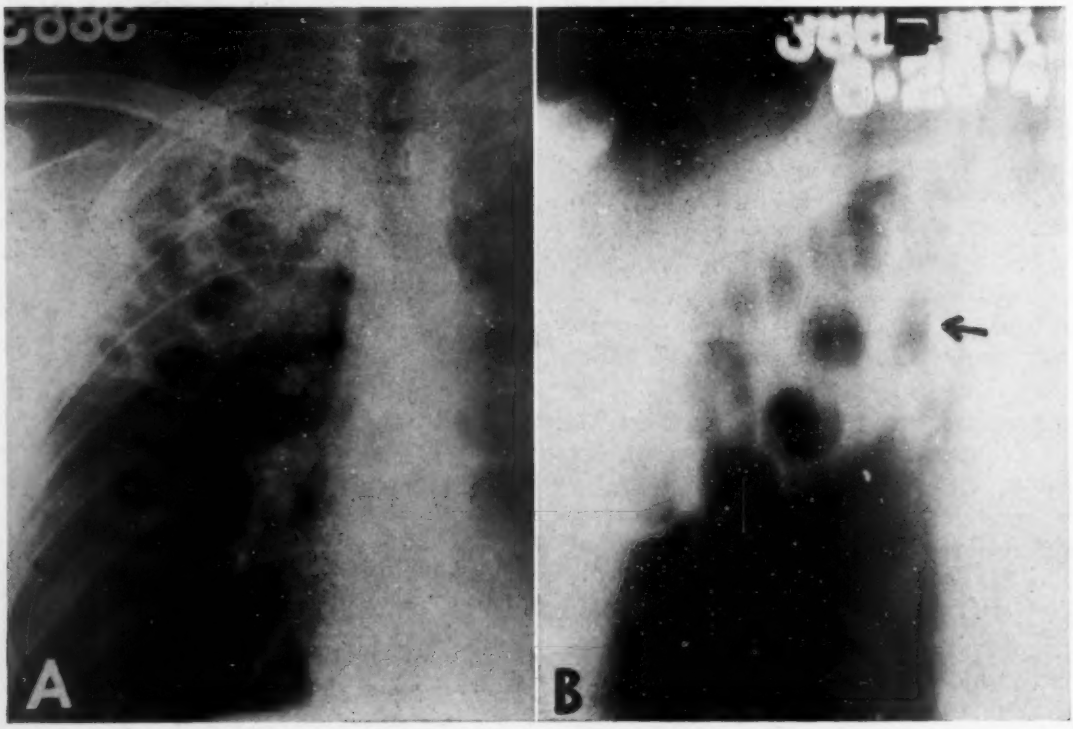


FIG. 2. Case II. *A*, extrapleural pack with residual cavity obscured by the lucite balls. *B*, planigram shows irregular cavity (arrow) medial to the perfectly spherical lucite balls.

Case iv. E. K., a veteran, aged thirty-three, who was diagnosed as having pulmonary tuberculosis of the right upper lobe in 1945. He gave a history of a shrapnel wound of the right chest in November, 1942, which had healed uneventfully. Sputum had become negative for tubercle bacilli in April, 1946, but he continued to have repeated hempotyses. Roentgen examination of the chest showed some strands of infiltration in the right supraclavicular region (Fig. 4*A*). Lipiodol studies showed no evidence of bronchiectasis. Planigrams showed an irregularly annular density just off the right hilum on the 5, 6, and 7 cm. films (Fig. 4*B*). However, it was not sharply delineated and its medial wall seemed to be formed by a branch of the pulmonary vessels. It was diagnosed as not being a cavity since it did not meet all the criteria. A right upper lobectomy was done April 10, 1947, because of the persistent hemoptyses and no definite cavity was found in the resected specimen.

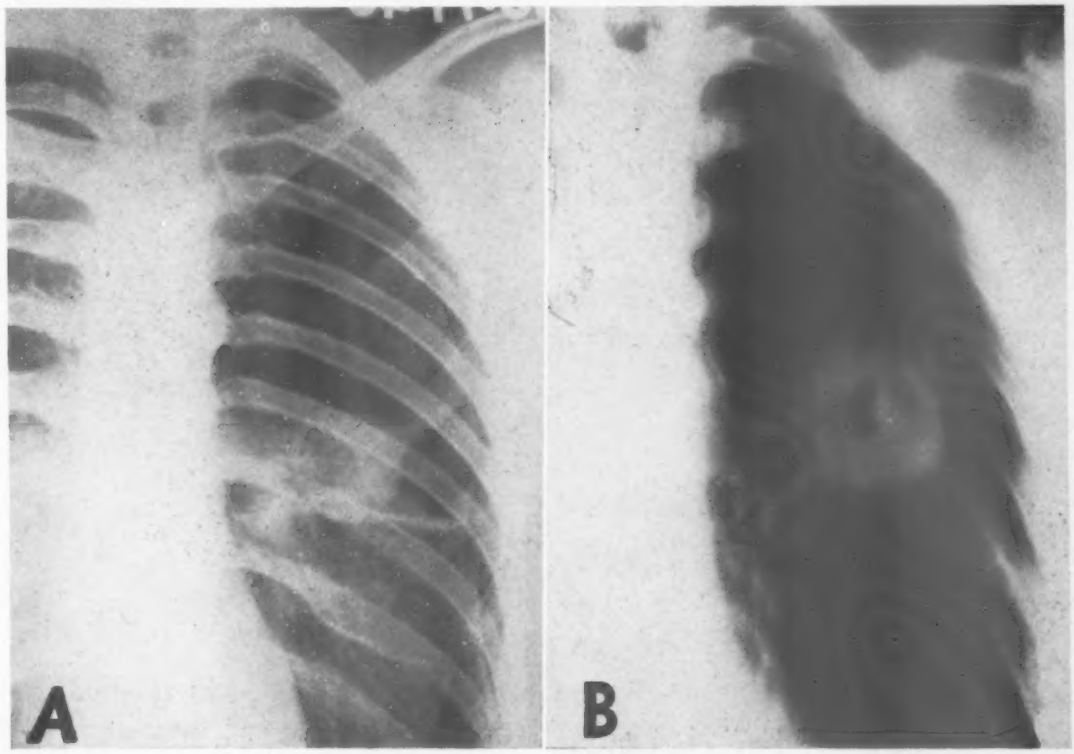


Fig. 3. Case iii. *A*, conventional film shows dense caseous area in left mid-lung field. *B*, planigram clearly shows the central area of rarefaction within the caseous mass. The resected lobe showed a hard cheesy sphere with a soft center containing greenish pus.

Case v. R. C., a veteran, aged twenty-eight, who had a seven-rib thoracoplasty on the right side for a large upper lobe cavity (Fig. 5*A*). Sputum, however, remained positive. Bucky film showed several suspicious but ill defined highlights within the dense right upper lobe (Fig. 5*B*). Planigrams revealed a well demarcated radiolucent area in the apical portion of the right upper lobe. It was seen clearly on the 6, 7, 8, 9, and 10 cm. levels and corresponded in location with the site of the original cavity. In addition, there was an irregularly oval radiolucent area in the basal portion of the right upper lobe just merging with the pleura (Fig. 5, *C* and *D*). However, it was not sharply delineated and did not correspond in location with any definite cavity prior to surgery. It was felt that this "highlight" represented normally aerated lung surrounded by thick pleura and areas of fibrosis. Lobectomy on January 23, 1947, proved this interpretation to be correct.

Case vi. H. B., a World War I veteran, aged fifty-two, with a history of pulmonary tuber-

culosis since 1927. A three-stage left thoracoplasty was done in 1944 for a large cavity in the left upper lobe (Fig. 6*A*). Sputum, however remained positive. On conventional chest film, details of the left lung were obscured by the very thick pleura. On the planigram, however, a large, irregular, radiolucent area was visible in the compressed left lung. A large bronchus could be seen leading directly into this area

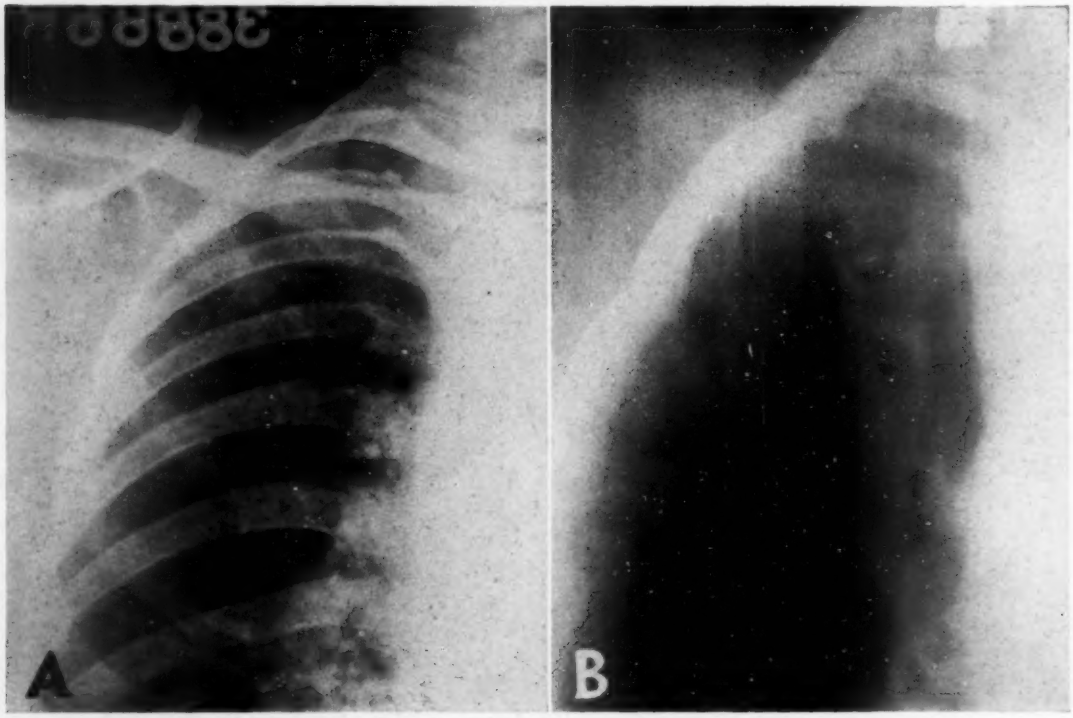


FIG. 4. Case IV. A veteran, aged thirty-three, with repeated hemoptyses. *A*, a few strands of infiltration are seen in the right infraclavicular region. Some old shrapnel fragments are noted in the right upper chest. *B*, planigram shows irregularly annular density just off the right hilum. Although it was seen at several levels, it was not sharply demarcated and seemed to be formed partly by vessel shadow. It was interpreted as not being a cavity. Confirmed at operation.

(Fig. 6, *B* and *C*). It was interpreted as a cavity. This was confirmed at pneumonectomy on June 17, 1947.

CASE VII. A. E., a colored male, aged thirty-two, diagnosed as having pulmonary tuberculosis in January, 1946. A roentgenogram showed a fibrocaseous lesion in the left upper lobe with a 2 cm. cavity in the left infraclavicular region (Fig. 7, *A* and *B*). A six-rib thoracoplasty was completed on November 29, 1946, and sputum has remained negative since that time (Fig. 7*C*). The original cavity in the left infraclavicular region can no longer be identified but a large, oval, radiolucent area is seen on several planigrams in the apical portion of the compressed left upper lobe (Fig. 7*D*). It does not correspond in location with any previous cavity and it is felt that it probably represents an area of normal lung surrounded by thick pleura and areas of fibrosis. The persistently negative sputum for eleven months with no change in the planigraphic appearance of the area over a period of six months supports this view.

CASE VIII. S. C., a male, aged thirty-three, who had a seven-rib thoracoplasty completed in January, 1947, for a large cavity in the right infraclavicular region (Fig. 8*A*). Sputum has been persistently negative since December, 1946. Planigrams, however, still reveal a small, well defined, radiolucent area measuring about 0.5 cm. in diameter situated just off the right hilum seen clearly on the 7, 8, and 9 cm. levels (Fig. 8, *B* and *C*). It is felt that this is not a residual cavity since it would be almost

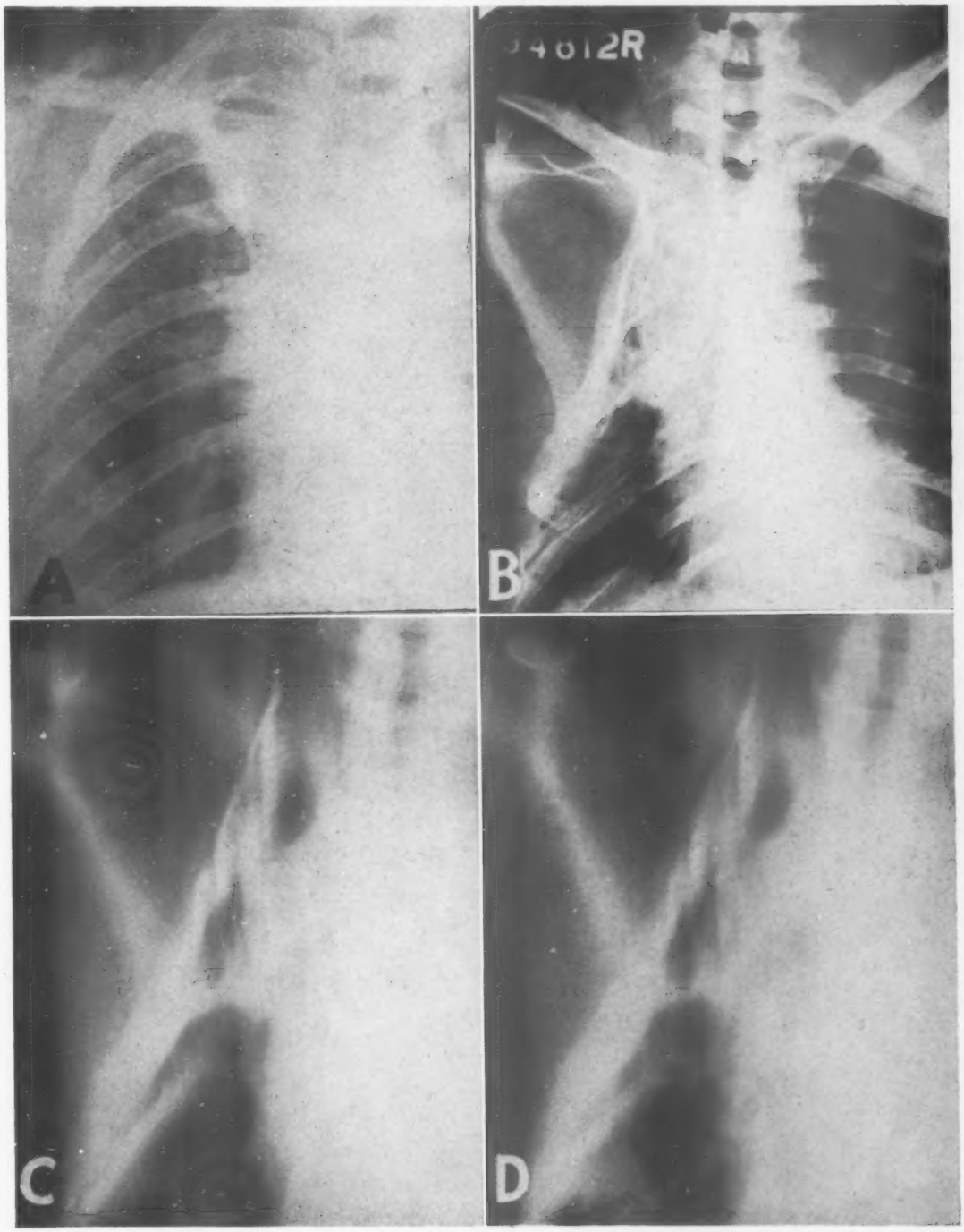


FIG. 5. Case v. *A*, admission film showing large cavity in right apex. *B*, Bucky film after seven-rib thoracoplasty. Sputum still positive. Many suspicious highlights are seen in dense right upper lung field. *C* and *D*, planigrams reveal well demarcated radiolucent area in apical portion of right lung which was seen clearly on 6, 7, 8, 9, and 10 cm. levels. It was interpreted as a cavity. The radiolucent area below this is not clearly demarcated, does not correspond in location with any previous cavity and is interpreted as representing normal lung surrounded by dense fibrous strands and thick pleura. Examination of the resected specimen following lobectomy confirmed this interpretation.

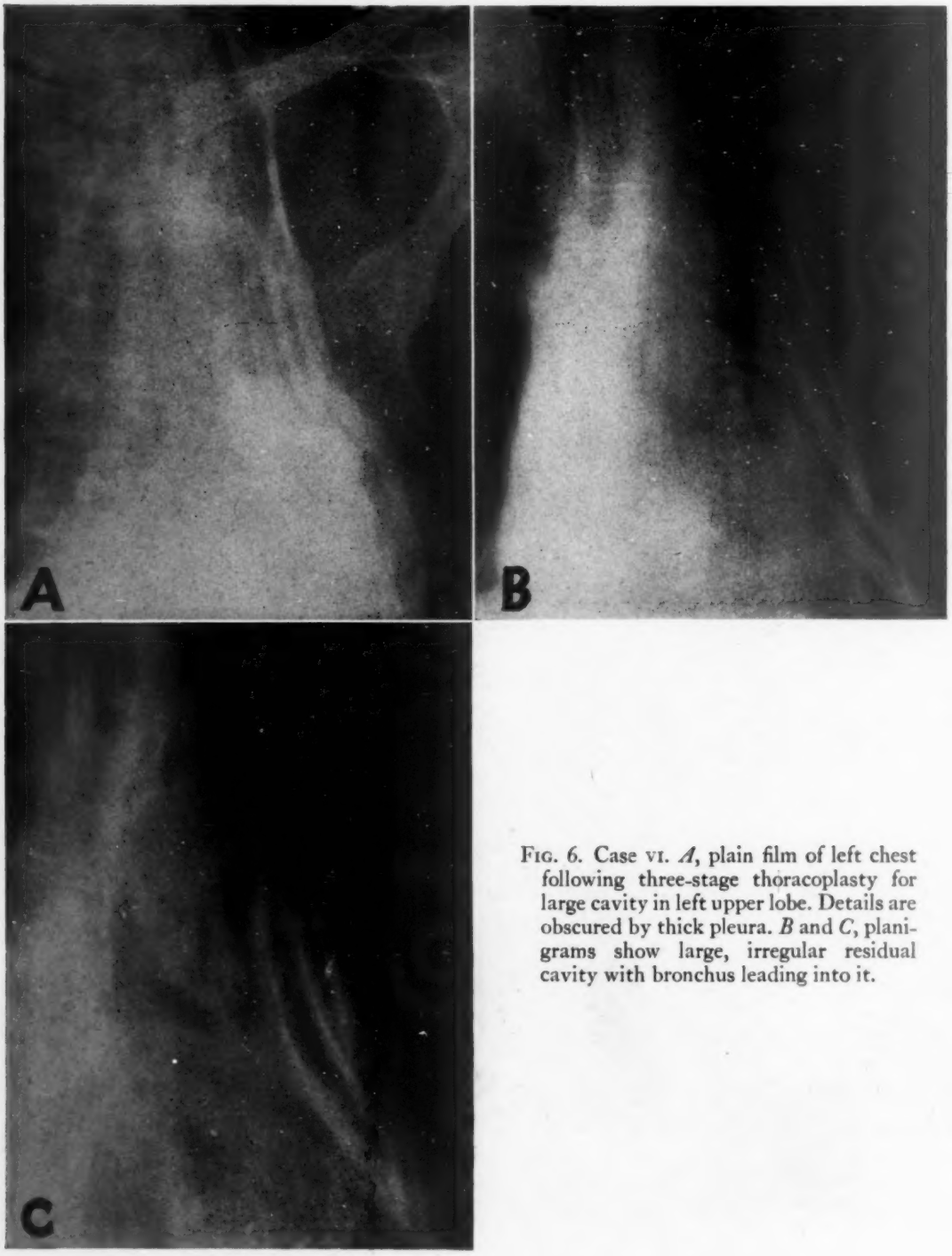


FIG. 6. Case VI. *A*, plain film of left chest following three-stage thoracoplasty for large cavity in left upper lobe. Details are obscured by thick pleura. *B* and *C*, planigrams show large, irregular residual cavity with bronchus leading into it.

impossible for a cavity as small as this to show on three consecutive levels 1 cm. apart. Furthermore, it does not correspond in location with the original cavity which was situated in the axillary portion of the lung field. The persistently negative sputum for eleven months supports this conclusion.

CASE IX. J. D. P., a patient aged twenty-five, with bilateral pulmonary tuberculosis. The

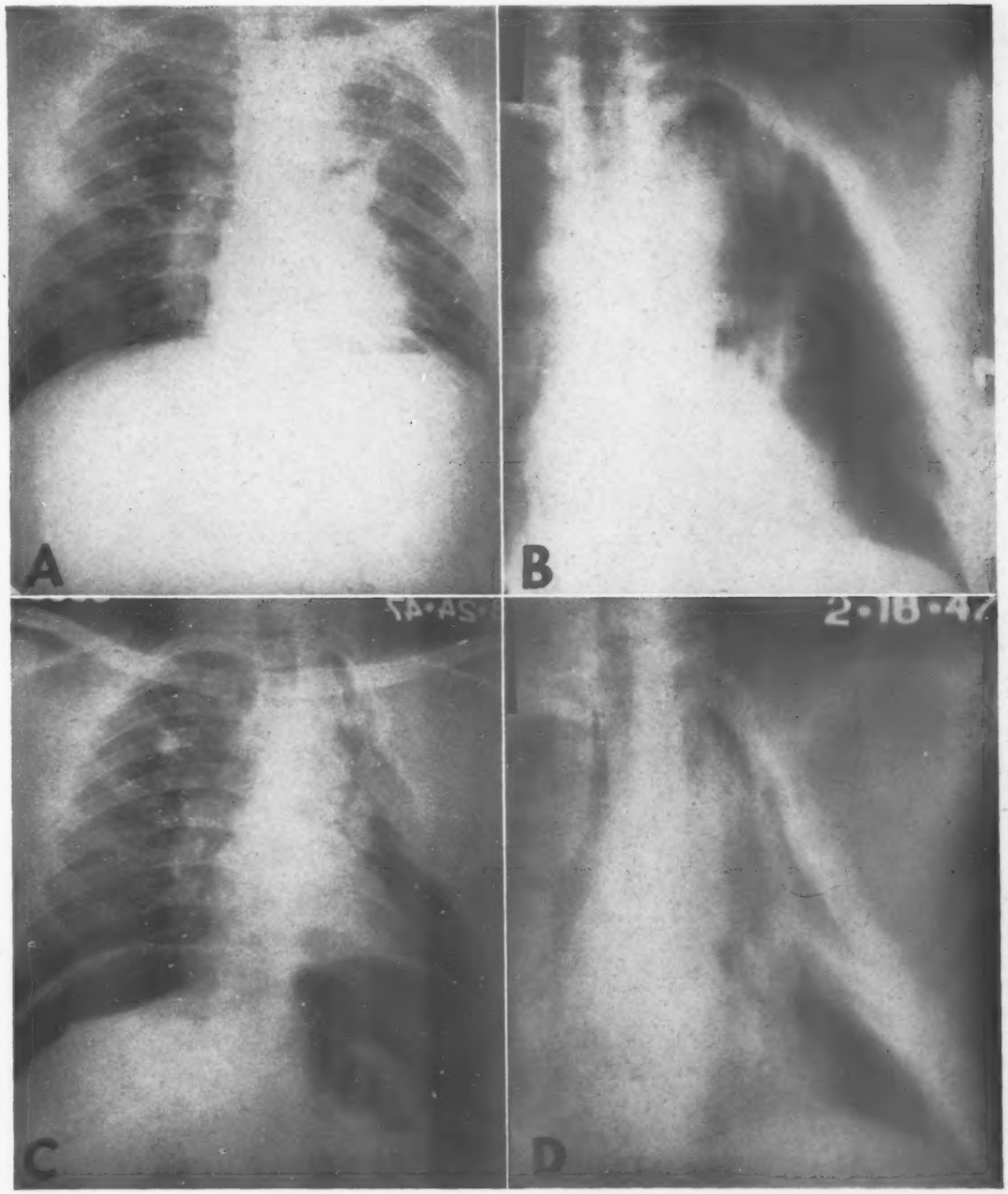


Fig. 7. Case VII. *A*, conventional film showing tuberculous lesion in left upper lobe. *B*, planigram showing definite 2 cm. cavity in left infraclavicular region. *C*, conventional chest film after left thoracoplasty. Patient also has pneumoperitoneum. *D*, planigram shows large radiolucent area in left apex. However, it does not correspond to location of original cavity and probably represents normally aerated lung surrounded by thick pleura and dense fibrous strands. Sputum negative for eleven months.

lesion in the left lung is controlled by pneumothorax. The lesion in the right upper lobe consists of multiple, irregular, caseous areas (Fig. 9*A*). Three sets of planigrams have failed to demonstrate any definite cavitation (Fig. 9, *B* and *C*). Sputum concentrates, however, are still alternately positive and negative for tubercle bacilli. This is the type of lesion in

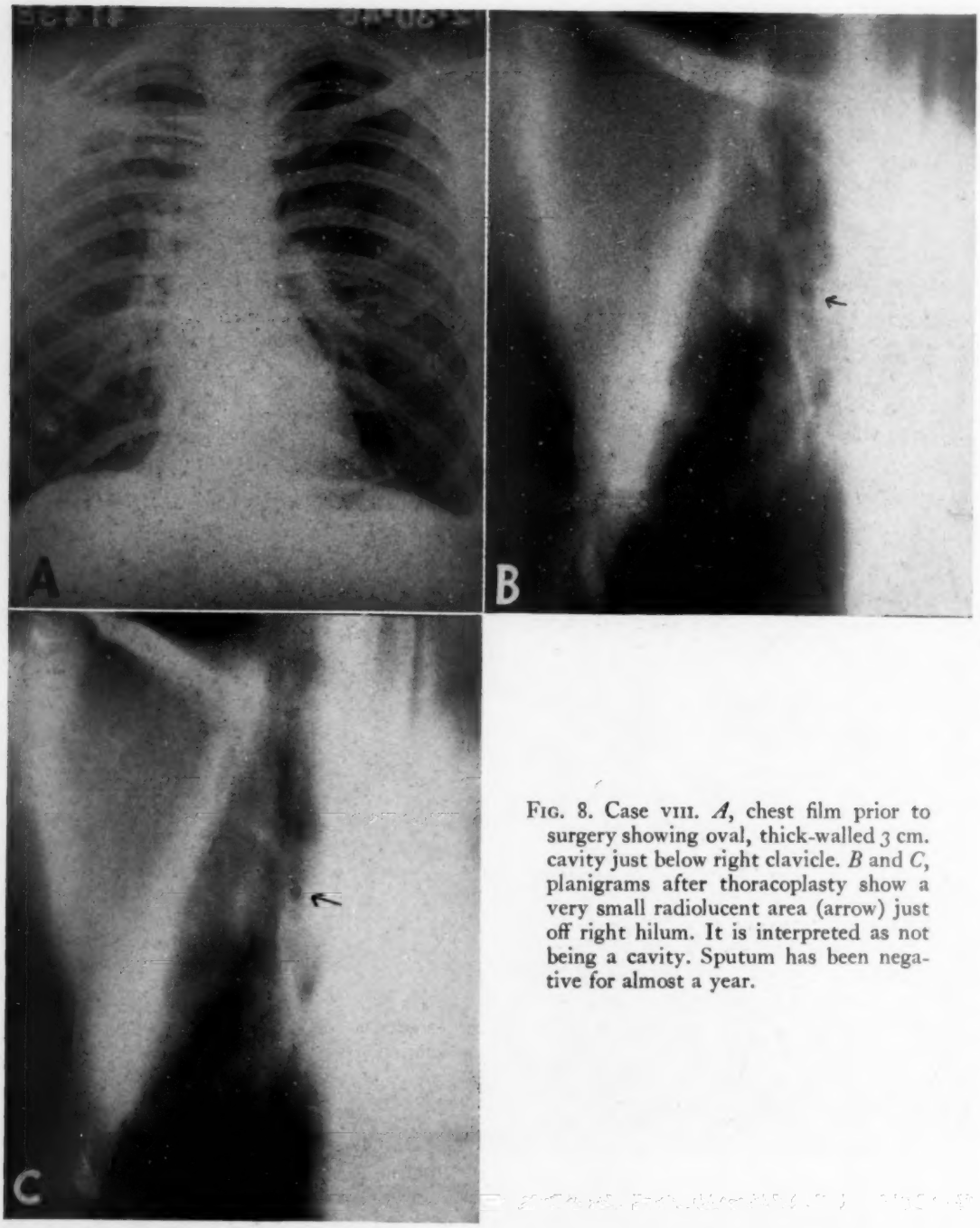


FIG. 8. Case VIII. *A*, chest film prior to surgery showing oval, thick-walled 3 cm. cavity just below right clavicle. *B* and *C*, planigrams after thoracoplasty show a very small radiolucent area (arrow) just off right hilum. It is interpreted as not being a cavity. Sputum has been negative for almost a year.

which we most often get equivocal results. The caseous foci may develop small central areas of liquefaction and discharge their contents into a bronchiole, but the resulting cavities are too small to be seen on the planigram. Sputum at this stage, if positive at all, will usually show tubercle bacilli only on concentrate or culture. Such microscopic or subclinical cavities may either close spontaneously or else they will enlarge, tubercle bacilli will multiply in the wall of the cavity, communication will be established with a larger bronchus and positive sputum on plain smear will result. In the latter case, the cavity usually becomes clearly visible on the planigram.

Case x. J. O., a male, aged twenty-three, who had a seven-rib thoracoplasty on the right side in 1945 for a cavity in the right upper lobe (Fig. 10*A*). A large residual cavity, however, could clearly be seen in the compressed lung (Fig. 10*B*). Revision operation was done in 1946 with resulting greater compression of the lung and "disappearance" of the residual cavity (Fig. 10*C*). Sputum, however, remained alternately positive and negative. Right pneumonectomy was done in April, 1947, and the resected specimen showed a slit-like cavity measuring 2.5 by 1.5 cm. in the compressed right upper lobe. Such flattened slit-like cavities may not show on the planigram unless some air gains access to the lumen.

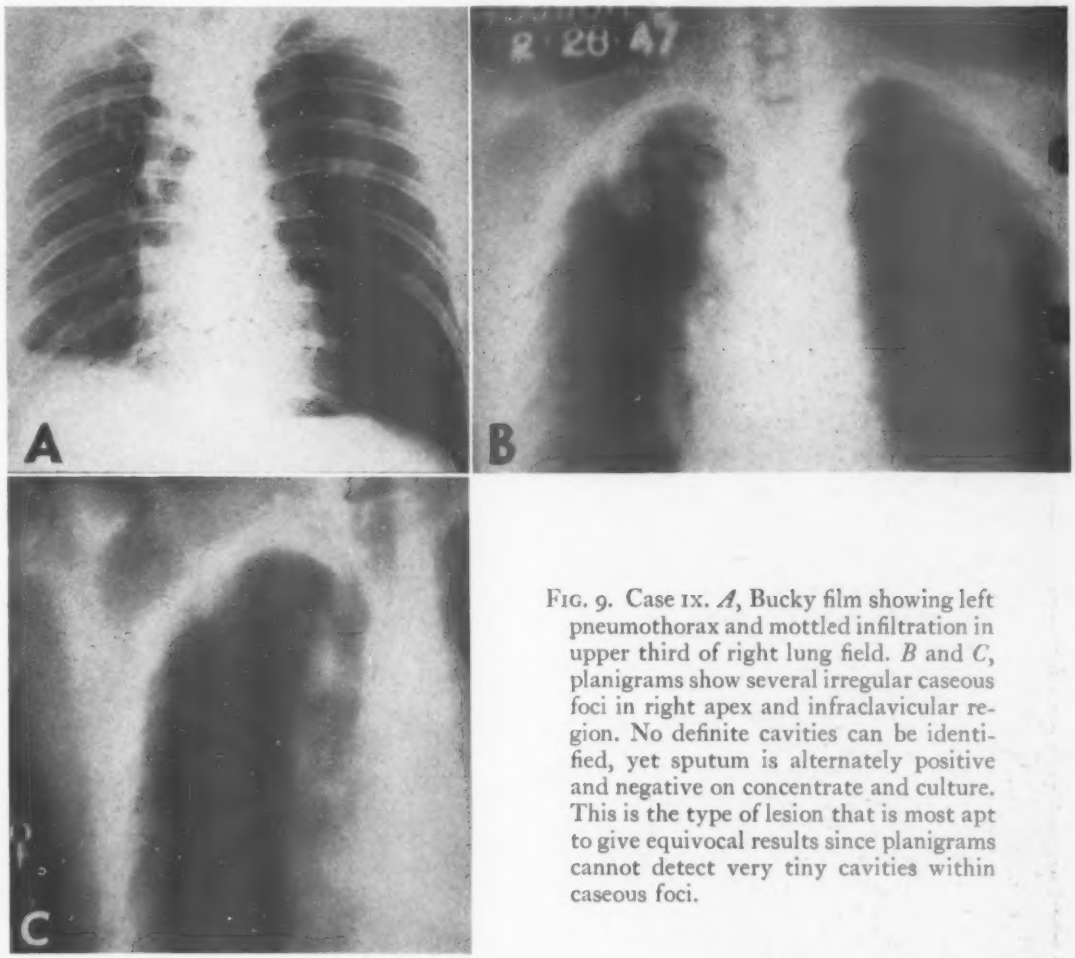


Fig. 9. Case ix. *A*, Bucky film showing left pneumothorax and mottled infiltration in upper third of right lung field. *B* and *C*, planigrams show several irregular caseous foci in right apex and infraclavicular region. No definite cavities can be identified, yet sputum is alternately positive and negative on concentrate and culture. This is the type of lesion that is most apt to give equivocal results since planigrams cannot detect very tiny cavities within caseous foci.

Case xi. J. F., a male, aged twenty-one. A six-rib right thoracoplasty was done in October and November, 1946, for a dense, fibrocaseous tuberculosis involving the entire right upper lobe (Fig. 11, *A* and *B*). Sputum continued positive on concentrate and culture and planigrams showed numerous small, oval, radiolucent areas within the dense, compressed right upper lobe (Fig. 11, *C* and *D*). The lung was resected July 29, 1947, and showed extensive fibrosis, scattered, small caseous areas and numerous thick-walled, dilated bronchi (Fig. 11*E*). The latter corresponded with the radiolucent areas seen on the planigrams.

In an extensive, caseous disease which undergoes fibrosis, it may be very difficult to distinguish between small residual cavities and bronchiectatic dilatations.

Case xii. J. T. C., a white male, aged forty-eight. Onset of his tuberculosis was in 1929.

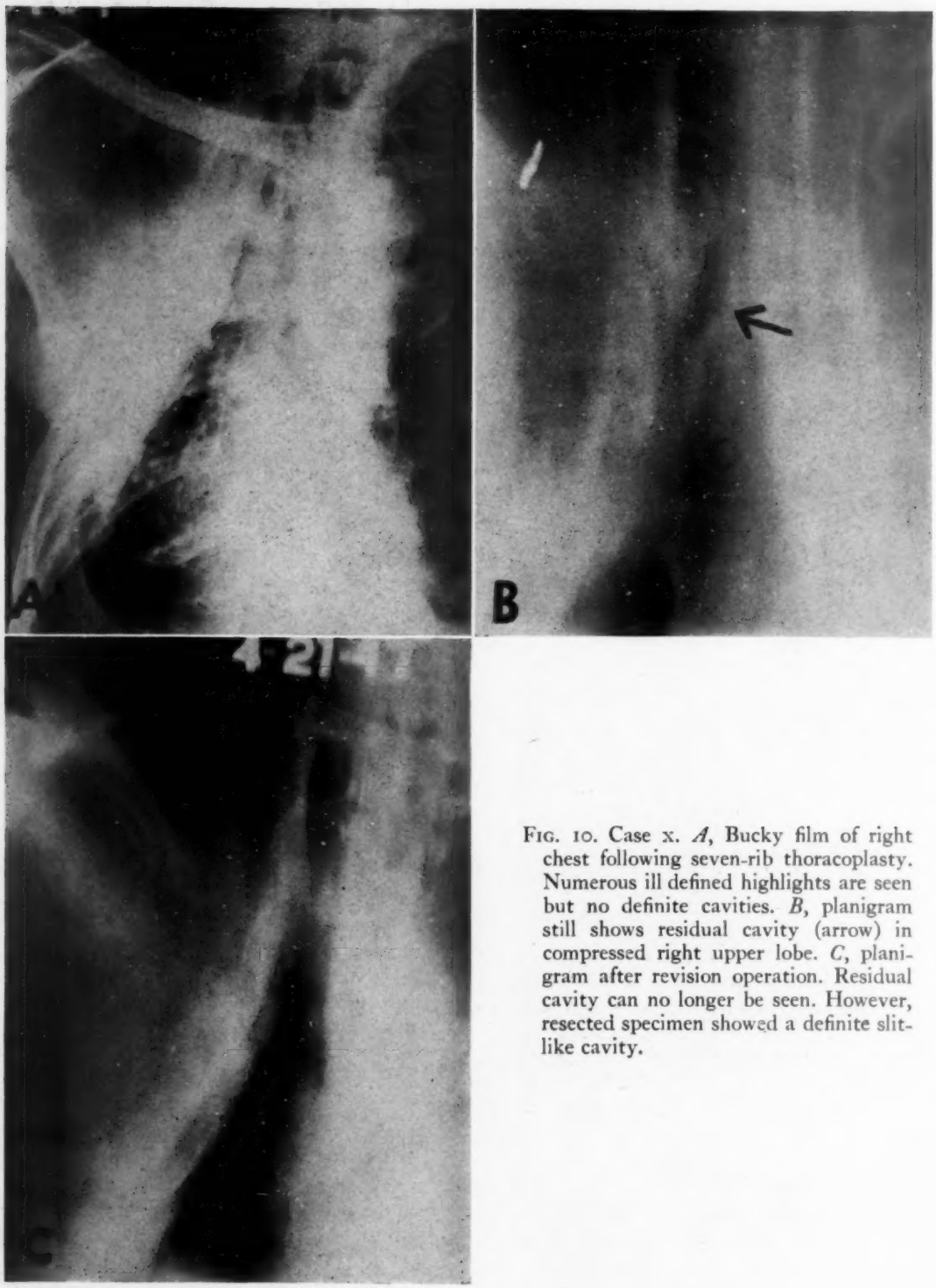


FIG. 10. Case X. *A*, Bucky film of right chest following seven-rib thoracoplasty. Numerous ill defined highlights are seen but no definite cavities. *B*, planigram still shows residual cavity (arrow) in compressed right upper lobe. *C*, planigram after revision operation. Residual cavity can no longer be seen. However, resected specimen showed a definite slit-like cavity.

Conventional chest film shows extensive fibrocalcific deposits in upper third of right lung field with shift of trachea and mediastinum toward the right side (Fig. 12*A*). Planigrams show two well defined radiolucent areas just beneath the apical pleura on the 5, 6, and 7

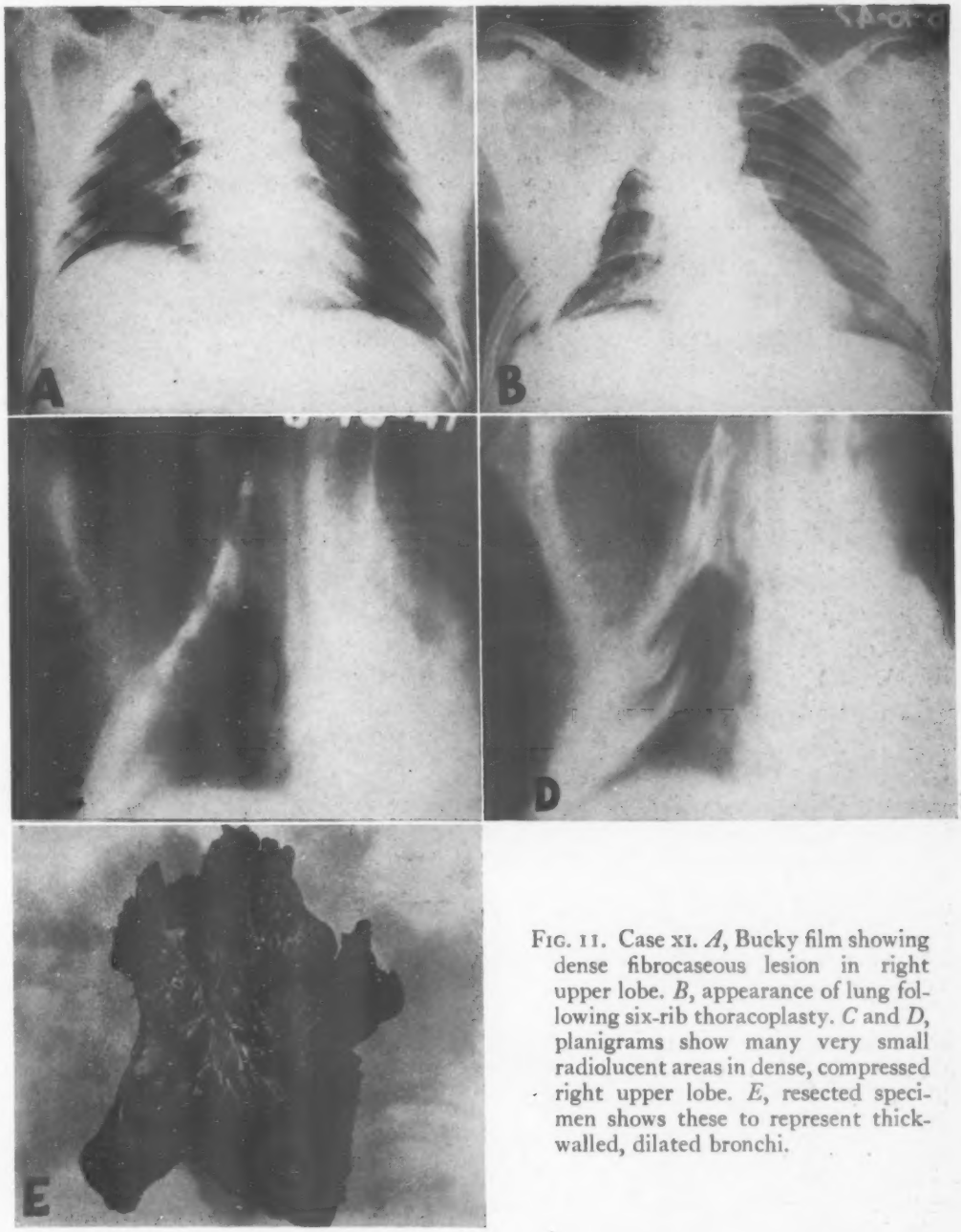


Fig. 11. Case xi. *A*, Bucky film showing dense fibrocaseous lesion in right upper lobe. *B*, appearance of lung following six-rib thoracoplasty. *C* and *D*, planigrams show many very small radiolucent areas in dense, compressed right upper lobe. *E*, resected specimen shows these to represent thick-walled, dilated bronchi.

cm. levels (Fig. 12*B*). Sputum has been persistently negative for tubercle bacilli since 1934. It is felt that these represent emphysematous blebs which are known to be fairly common in this location in cases of long-standing fibrosis.

Case xiii. F. P., a white male, aged fifty-three, admitted to Oteen in April, 1947, because of dyspnea and productive cough. Pulmonary tuberculosis was diagnosed in 1921 at which time he had a right thoracotomy for an empyema with bronchopleural fistula. Sputa were all negative for tubercle bacilli at that time and at several subsequent hospital admissions. Plain film showed dense fibrosis in the right apex and infraclavicular region with irregular calcification of the pleura in the right

mid-lung field (Fig. 13*A*). Planigrams revealed several sharply circumscribed, round, radiolucent areas within the dense right upper lung field (Fig. 13*B*). Lipiodol instillation demonstrated saccular bronchiectasis in this region (Fig. 13*C*). The radiolucent areas probably represent areas of emphysema adjacent to the bronchiectatic dilatations. The negative sputum since 1921 is the deciding factor in a case like this.

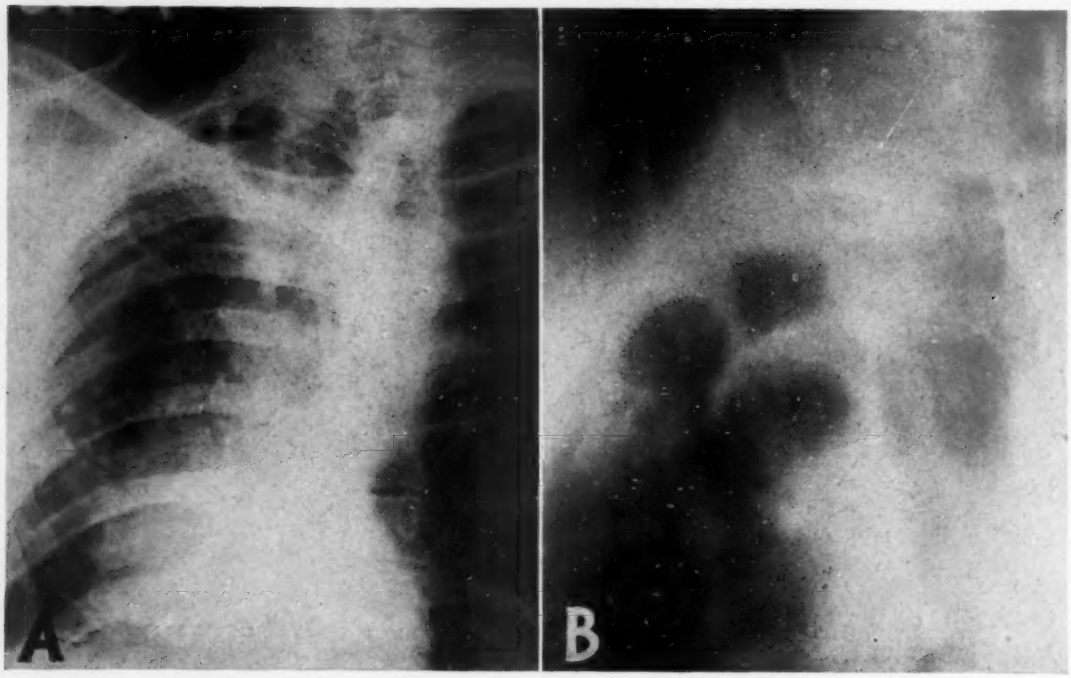


FIG. 12. Case XII. *A*, a case of long-standing tuberculosis. Plain chest film shows extensive fibrocalcific deposits in right lung with several suspicious highlights in right apex. *B*, planigram shows two well defined, radiolucent areas beneath apical pleura. Sputum negative since 1934. They are interpreted as emphysematous blebs.

CASE XIV. G. G., a white male, aged fifty-four. Onset of his tuberculosis was in 1923. Conventional film shows dense fibrosis in the left upper lobe with many ill defined highlights (Fig. 14*A*). Planigrams reveal many large, well demarcated, thin-walled radiolucent areas within the fibrotic left upper lobe (Fig. 14*B*). Sputum has been persistently negative since January, 1946. The radiolucent areas are interpreted as areas of emphysema rather than tuberculous cavities.

CASE XV. S. B., a white male, aged fifty. Onset of his tuberculosis was in 1939 at which time a roentgenogram showed a fibrocaseous tuberculosis involving the entire right upper lobe with several definite areas of cavitation. Patient has refused any collapse therapy. Over a period of eight years there has been marked fibrosis of the lesion with contraction of the right upper lobe (Fig. 15*A*). However, sputum is still persistently positive and planigrams show several radiolucent areas which are interpreted as probable cavities (Fig. 15*B*).

This is another case where differentiation between small residual cavities and bronchiectatic dilatations is difficult. The sputum findings are important.

## COMMENT

Unfortunately there is no single method of roentgen examination which will accurately diagnose pulmonary cavitation in 100 per cent of cases. We have had considerable experience with Bucky technique and more limited experience with stereoscopic films, and it is our opinion that

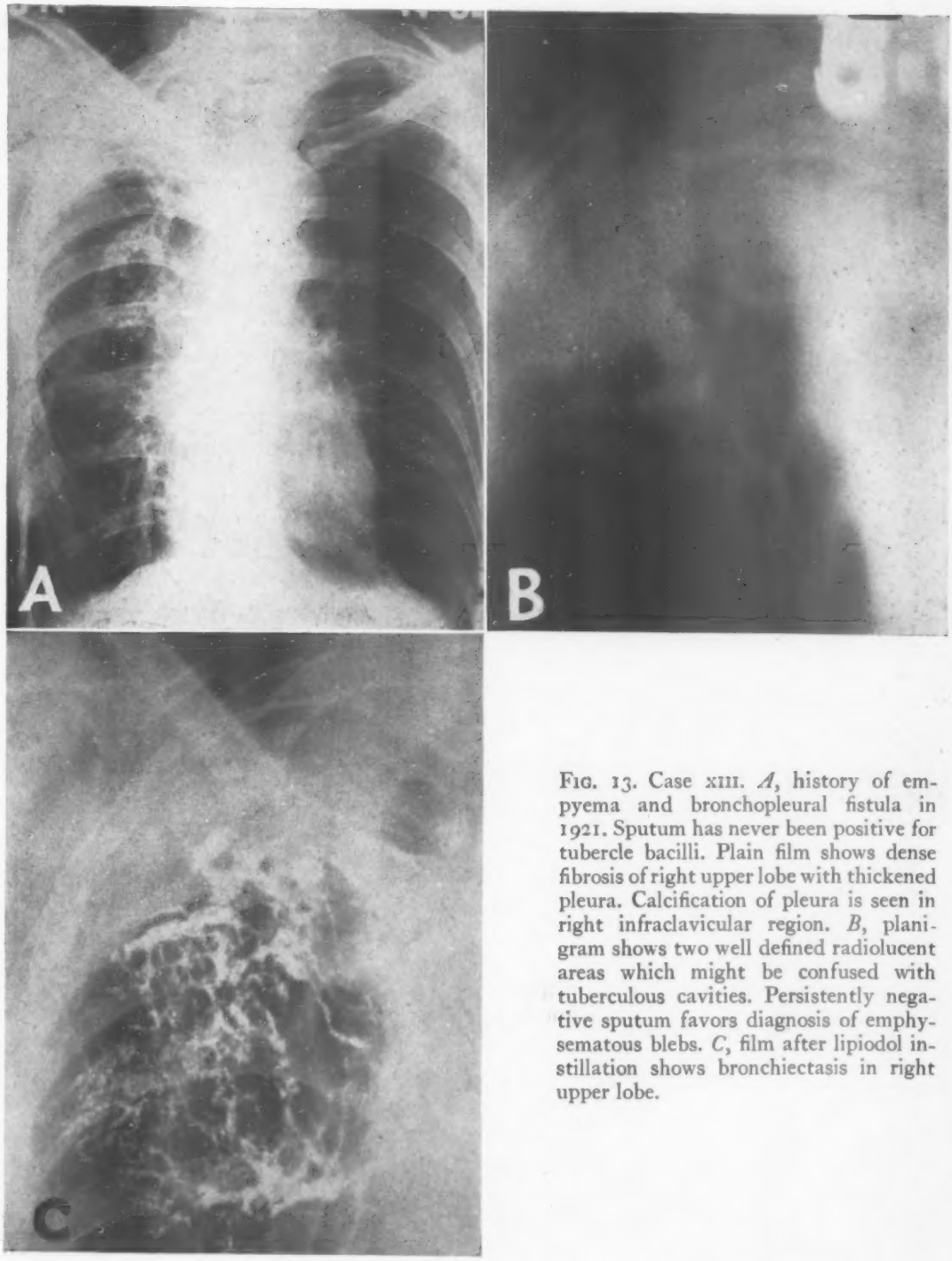


FIG. 13. Case XIII. *A*, history of empyema and bronchopleural fistula in 1921. Sputum has never been positive for tubercle bacilli. Plain film shows dense fibrosis of right upper lobe with thickened pleura. Calcification of pleura is seen in right infraclavicular region. *B*, planigram shows two well defined radiolucent areas which might be confused with tuberculous cavities. Persistently negative sputum favors diagnosis of emphysematous blebs. *C*, film after lipiodol instillation shows bronchiectasis in right upper lobe.

planigraphic examination is superior to either of these methods. This is particularly true in dense caseous lesions or post-thoracoplasty lungs. Considering all types of tuberculous lesions, planigrams will correctly diagnose the presence or absence of cavitation in about 85 per cent of cases, if the criteria outlined above are used. For

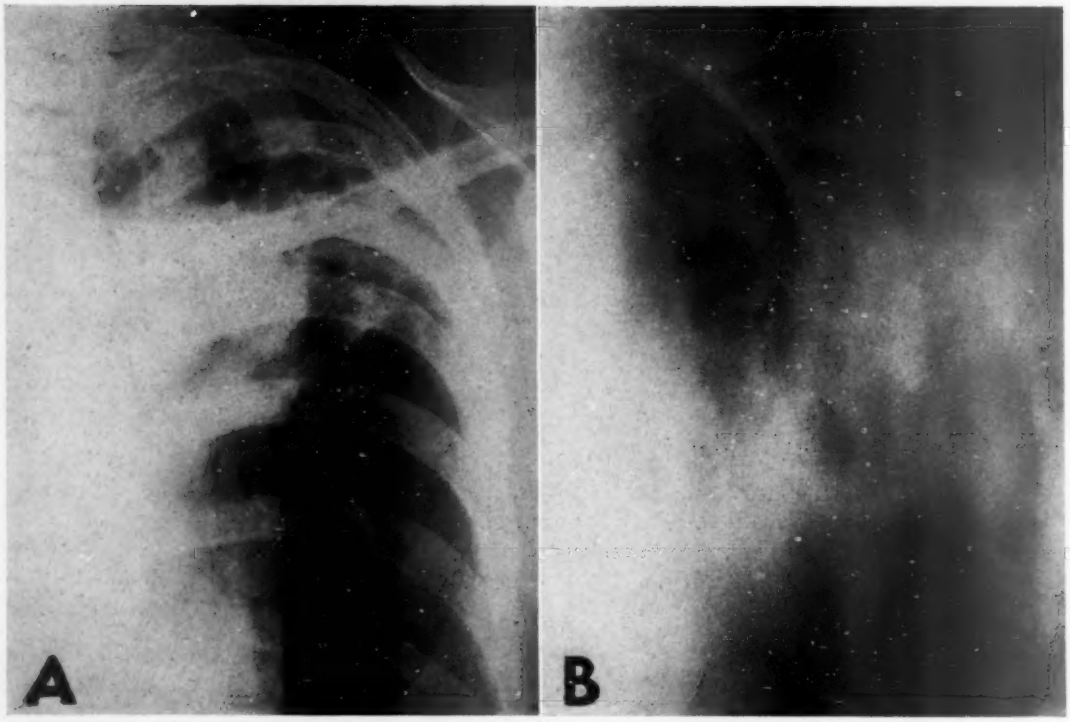


FIG. 14. Case XIV. *A* and *B*, another case showing similarity of emphysematous areas to tuberculous cavities in a fibrotic lung. Sputum in this case has been persistently negative for twenty-two months.

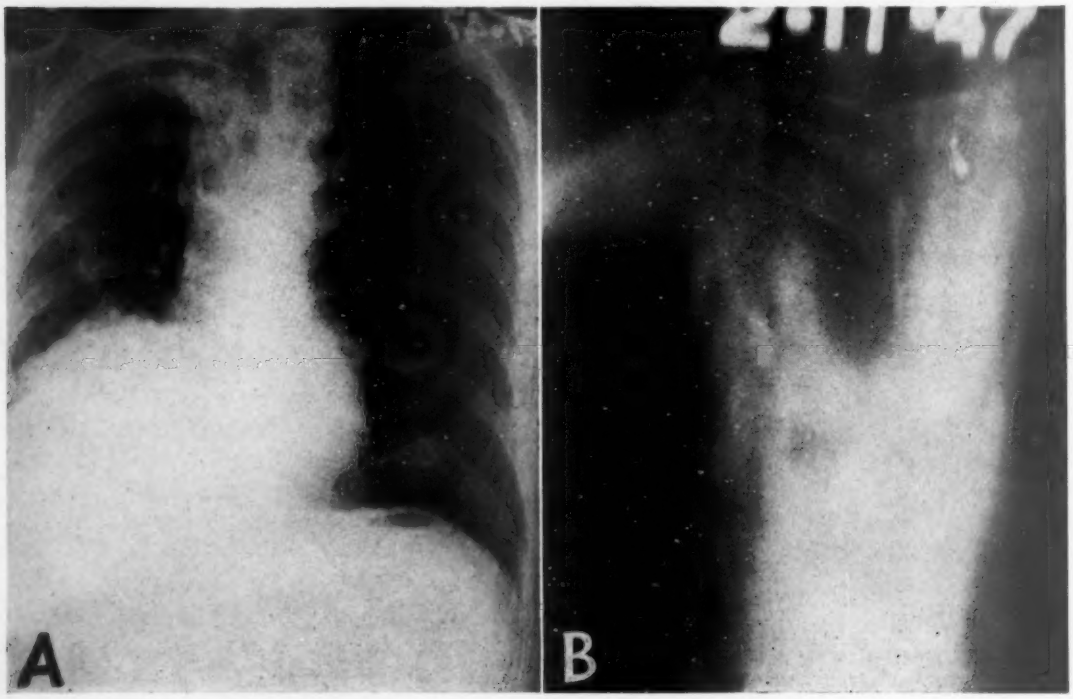


FIG. 15. Case XV. *A* and *B*, persistently positive sputum in a patient with a fibrocaseous lesion of right upper lobe undergoing gradual fibrosis over a period of eight years. Planigrams show many highlights within the shrunken right upper lobe. Final differentiation between tuberculous cavities and bronchiectatic dilatations can only be made by sputum studies.

the remaining 15 per cent which are inconclusive, we must rely on roentgenoscopy, sputum studies and clinical findings to make the decision.*

SUMMARY

1. Three hundred sets of planigrams in cases of pulmonary tuberculosis were studied with a view toward more accurately diagnosing cavitation by correlation with clinical and pathological data. Twenty-three cases had pulmonary resection and the roentgen shadows could be checked with the actual lung findings.

2. Certain rigid criteria are outlined for the interpretation of cavitation on planigrams and these are illustrated by case reports.

3. The limitations of planigams are discussed and some of the pitfalls in diagnosis are indicated. Particular emphasis is placed on emphysematous blebs and bronchiectatic dilatations which may be extremely difficult to distinguish from small tuberculous cavities. In such cases the sputum and clinical findings are of the utmost importance in differentiation.

Philip Morgenstern, M.D.
Veterans Administration
Oteen, N. C.

* Since the submission of this paper for publication we have examined an additional 27 cases whose films could be correlated with resected lung specimens. Our conclusions were essentially the same as those reached in our paper.

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# THE SYNDROME OF ARTERIOVENOUS FISTULA OF THE LUNG

*By* PETER CRANE, M.D., HENRY H. LERNER, M.D., *and* EDWIN A. LAWRENCE, M.D.

THE presence in the lung of an abnormal communication between an artery and a vein produces a clinical syndrome consisting of cyanosis, clubbing of the fingers and toes, bruit, and polycythemia.

The literature is extremely sparse in its reference to vascular tumors in the lung. There are twenty-four sporadic reports up to September, 1947, referring to 26 cases of vascular anomalies or new vascular growths in the lung with related clinical symptoms. It is interesting that in the last twelve months alone 8 new cases have been reported. A few others have been diagnosed but not reported, while many are not recognized. One of us (H. H. L.) has seen 3 surgically proved cases in the past three years.

It is quite probable that patients presenting these findings are mistakenly considered to be suffering from an incurable cardiac anomaly. Many instances of tumors of the lung masquerade under the stigma of congenital heart disease. The difficulty in making the correct clinical diagnosis might be overcome if the roentgenological and clinical features of the syndrome were more widely known. Attention should be called to the possibility of a vascular anomaly of the lung in any patient with unexplained polycythemia and associated symptoms due to disturbed oxygenation of the blood.

## DEFINITION AND NOMENCLATURE

The abnormal vascular communication in the lung has been designated by a variety of terms. Similar terms have been used to describe different pathological conditions. Conversely a single pathological condition has been designated by different names. The nomenclature of the vascular tumors as reported in the literature is unsatisfactory because of the scarcity of adequate pathological descriptions.

In this category is an early group of 9 cases diagnosed at autopsy (Table 1). The terms used include: Case 1—"capillary hemangioma." Case 2—"capillary type of malignant hemangioma." Case 3—"cavernous sinus spaces with cellular malignant areas." Case 4—"hemangioma." Case 5—(not recorded). Cases 6 and 7—"capillary angioma." Case 8—"cavernous hemangioma." Case 9—"closed hemangioma."

In a later group of 7 cases 4 (11, 13, 19, 22) were not proved either by operation or autopsy so that the final diagnosis cannot be recorded. In the remaining 13 cases the following terms were used: Case 10—"multiple hemangioma." Case 12—"cavernous hemangioma." Case 14—"cavernous hemangioma." Case 15—"arteriovenous fistula." Case 16—"multiple arteriovenous fistulae." Case 17—"cavernous hemangioma." Case 18—"arteriovenous aneurysm associated with congenital abnormalities of the pulmonary vessels." Case 20—"hemangioma." Case 21—"hemangioma." Case 23—"cavernous angioma." Case 24—"pulmonary arteriovenous fistula." Case 25—"pulmonary aneurysm." Case 26—"varicose vessels and sinuses."

When blood flows directly from an artery to a vein through widened vascular channels without an intermediate capillary bed the short circuit is referred to by some authors as an "arteriovenous aneurysm." This term is used by other authors as synonymous with "arteriovenous fistula". A distinction should be made between the two terms. An "arteriovenous fistula" is a direct shunt between an artery and a vein without the interposition of capillaries. An "arteriovenous aneurysm" is the result of a simultaneous rupture of an artery and a vein with the blood from both being poured out into the cellular tissues which forms a communication or "false aneurysm" between them.

In this paper we are including those cases in which a shunt exists between the arterial and venous systems of the pulmonary circulation. The case we are reporting we prefer to call an "arteriovenous fistula".

## HISTORICAL

Rodes[20] may be credited as the first to correlate the clinical picture with the pathological findings in the lung. His recognition and description of this syndrome was based on the postmortem examination of a patient who during life had manifested symptoms attributable to a vascular shunt. At autopsy "multiple multilocular hemangiomata" were found in the lungs.

Prior to the paper of Rodes in 1938 there were only four references in the literature dealing with vascular tumors of the lung. These were all necropsy reports. Plaut[18] states that de Lange and de Vries-Robles[14] in 1923 mention the first recorded autopsy case of "multiple capillary angiomas" of the lung. Wollstein[24] reported what she called a "capillary type of malignant hemangioma" in a four month old infant who had marked attacks of wheezing with groaning and cyanosis. Hall[10] reported a case with multiple cavernous sinus spaces in the lungs showing cellular malignant areas. Bowers[4] reported an autopsy on a two day old male infant with numerous hemangiomata of the lung.

Following Rodes' report nineteen other papers have appeared reporting one or more instances and bringing the total number of cases to 26. Duvoir *et al.*[7] performed a necropsy on a twelve year old child who had multiple visceral angiomata, one being in the lung. Plaut's[18] report of 2 autopsies mentions "capillary angioma." Verse[23] reported 2 autopsied cases. One was in a male infant who had "multiple cavernous hemangiomas" of the left lung. The second was in a female who had a "closed hemangioma" of the lung. She was known to have had "heart disease" for a period of at least three years.

The 4 cases appearing prior to Rodes' report and the 5 cases noted in the preceding paragraph have such meager clinical and laboratory data that they could not be in-

TABLE I

INCOMPLETE CASES

| Case No. | Author | Sex | Age | Cyanosis | Dyspnea | Pathology |
|---|---|---|---|---|---|---|
| 1 | de Lange and de Vries-Robles 1923—autopsy | F | 2½ mo. | | | Capillary hemangioma |
| 2 | Wollstein 1931—autopsy | F | 4 | Yes | Yes | Capillary hemangioma (malignant) |
| 3 | Hall 1935—autopsy | F | 40 yr. | Terminally | | Cavernous sinus spaces (malignant) |
| 4 | Bowers 1936—autopsy | M | 2 days | | Yes | Hemangioma |
| 5 | Duvoir *et al.* 1939—autopsy | | 12 yr. | | Yes | |
| 6 | Plaut 1940—autopsy | F | 35 | Slight | | Capillary angioma |
| 7 | Plaut 1940—autopsy | F | 53 | | | Capillary angioma |
| 8 | Verse 1943—autopsy | M | Infant | | Sudden | Cavernous hemangioma |
| 9 | Verse 1943—autopsy | F | 30 | | | Closed hemangioma |

cluded in our statistical analysis. Their salient features are therefore outlined in Table 1.

Rodes' paper, which was the first to correlate the clinical with the pathological findings, was based on the autopsy of a twenty-five year old male with multiple multilocular hemangiomata in both lungs. The patient died of a massive pulmonary hemorrhage. The first clinical diagnosis of an arteriovenous fistula was made by Smith and Horton.[22] They reported a case of a forty year old male in whom they were able to demonstrate an arteriovenous fistula of the lung by means of angiocardiography. They were unable to obtain pathological proof of their diagnosis. Hepburn and Dauphinee[11] must be credited with the first case diagnosed clinically and proved at surgery. They reported a twenty-three year old female who had an hemangioma in the upper part of the right lower lobe of the lung. This was diagnosed as a "sinus cavernous angioma" and confirmed by pneumonectomy. Goldman[8] reported a case of a twenty-two year old male who was clinically diagnosed as having a "cavernous hemangioma" of the left midlung field. In this report he gives a complete description of the clinical syndrome and the diagnostic roentgenologic criteria. He mentions the presence of a large vascular tumor mass in the lung parenchyma from which large blood vessels lead to the hilum of the lung. Janes[12] reported a thirty year old male diagnosed as having cavernous hemangiomas of the right and left lung fields and proved by surgery. Jones and Thompson[13] reported a twenty-four year old female with varicosities of the right upper lobe and an arteriovenous fistula demonstrated at operation and by specimen. Adams *et al.*[1] reported a twenty-four year old male in whom a pneumonectomy was done for a multilocular smooth-lined cavity with arteriovenous connections or arteriovenous fistulae. Alexander[2] reported the autopsy findings in a forty-one year old male with cavernous hemangiomas which connected directly with the pulmonary vessels. Sisson, Murphy and Newman[21] reported a case of a forty-five year old female who had arteriovenous aneurysms in the right and left lower lung fields. These were diagnosed as arteriovenous fistulae by angiocardiography and proved at autopsy. Lindren[15] reported 3 cases of arteriovenous fistula. The first was in a thirty year old male who had an arteriovenous communication in the region of the left interlobar fissure. The second was in a twenty-nine year old male who had hemangiomas in the right and left lung fields. The third was in a twenty-five year old female who had four vessels leading to a large tumor in the left lingula. Angiocardiography with lobectomy was performed in the latter two. The first case had no pathological confirmation. Makler and Zion[16] reported a case of multiple pulmonary hemangiomas in a twenty year old male. Surgical proof of an arteriovenous fistulae was not available. Goldman[9] reported 2 cases of arteriovenous fistulae in brothers and pointed out that it may be familial. (One of these might be the case reported in 1943.) Beierwaltes and Byron[3] reported a single case of an arteriovenous aneurysm. Burchell and Clagett[6] reported a case of an arteriovenous fistula complicated by collateral circulation and cured by lobectomy.

The case reported in this paper was diagnosed clinically and roentgenologically prior to surgery. Angiocardiography and surgery demonstrated the lesion to be vascular in nature. Histopathological examination proved it to be an arteriovenous fistula.

## CASE REPORT

*Present Illness.* This fifty year old white male, railroad shop worker, had a routine preemployment physical examination and chest roentgenogram about November 24, 1946. At that time he was told that he had a large tumor of the right lung and was advised to consult his physician.

He had always been well. There was no history of cough, hemoptysis, weight loss or fever. On rare occasions he had noted constricting pain lasting about one or two minutes, radiating from the middle of the right chest

across to the right side. These pains were not related to exertion, the intake of food, or any unusual position of the body. They did not radiate to the arms, back or neck. The last episode of pain occurred one and one-half months previous to entry into hospital.

*Physical Examination.* General: Well-nourished, middle-aged, white male, in no distress. Feet and hands are visibly cyanotic. Head: Normal in contour. No irregularities, scars or tumors. Eyes: Small pterygium, left. Ears: Hearing appears normal. No discharge. Nose: Septum straight. No obstruction. Throat: Pharynx granular. Neck: Thyroid not palpable. No pulsations. Cardiovascular: Blood pressure 110/70. Dull to percussion anteriorly below the fifth right rib, with decreased breath sounds and vocal fremitus. There is a very loud systolic bruit over this area. Few dry crackling rales at both bases posteriorly. Chest: Expansion is free and equal. Resonance and fremitus not increased or diminished. Vesicular breath sounds heard throughout. No rales. Expiration not prolonged. Gastrointestinal: Mouth—teeth carious and dirty with marked pyorrhea. Abdomen: Soft. No masses, rigidity, or tenderness. Liver, spleen and kidneys are not palpable. No hernias. Appendectomy scar. Rectum: No induration, hemorrhoids, fissures or fistulas. Genitourinary: Discrete, rubbery, nontender, translucent 3 cm. mass at upper pole left testicle. Neuropsychiatric: Mentally clear. No tremors. Superficial and deep reflexes are present and active. Babinski and Romberg signs negative. No clonus. Skin and Mucous Membranes: Lips and mucous membranes cyanotic. Numerous small petechiae on lower legs. Extremities: Slight clubbing of fingers and toes. Moderate varicosities on both legs. No ankle edema. Bones and Joints: Spine is straight and flexible. No pain on motion or percussion.

Diagnosis: (1) Hemangioma of right lung, right middle lobe. (2) Hydrocele, left. (3) Chronic sinusitus. (4) Pyorrhea.

*Operative Report:* (Doctor E. Lawrence). A curvilinear incision was made over the right chest following the fourth rib. Periosteum was reflected with a periosteal elevator and the rib removed from its sternal junction posteriorly to near its vertebral origin. Pleura was then opened and the tumor in the right middle lobe exposed. The right upper and middle lobes were then removed as follows: Sharp dissection was used to isolate the branches of the pulmonary arteries and vein. These were then doubly ligated, transfixed, and cut. The right upper and middle bronchi were then exposed and severed near their origin. The open proximal ends were then closed with interrupted silk sutures. Hemostasis was obtained by clamp and ligature, and the thoracic cavity washed out with normal saline. A No. 24 French catheter was then sutured to the parietal pleura and brought out through the wound for closed drainage. Two hundred thousand units of penicillin was placed in the pleura cavity. Pleura was then closed. Muscles and skin were closed with interrupted silk. The thoracic cavity was then aspirated of all air with a syringe in order to reinflate right lower lobe.

*Pathological Report: Gross:* This specimen consists of the upper and middle lobes of a right lung, amputated at the hilum. The interlobar fissure is obliterated by dense, old, fibrous adhesions in its ventral one-third. In its dorsal two-thirds there are delicate fibrous adhesions between the two lobes. The upper lobe measures about 15 by 11 by 6 cm. The middle lobe measures about 12 by 7 by 5.5 cm. Much of the lower lobe is occupied by a bulging cystic tumor which borders upon the interlobar fissure, extending to within about 3 cm. of the ventral margin and about 2 cm. of the posterior border. The surface of the cyst bulges prominently on the lateral surface of the lower lobe and its wall is so thin that in places it is transparent. On its superior surface the cyst encroaches slightly upon the parenchyma of the upper lobe, compressing it. On the medial surface there is a smooth elevation, apparently consisting of atelectatic lung which is compressed by the medial surface of the cyst. The pleura of the subapical portion of the lung on its dorsal surface is thickened and unevenly hemorrhagic. Numerous small fibrous tags are attached to the pleural surface in this portion over an area which measures about 8 by 5.5 cm. in diameter and located principally on the posterior and posterolateral surface of the upper lobe. Elsewhere the pleura is thin, transparent and slightly wrinkled. It is unevenly mottled and streaked with black pigment. The peribronchial lymph nodes at the hilum are not appreciably enlarged; they are firm and black. The larger vessels at the hilum are ligated with surgical sutures.

A vertical section taken through the center of the bulbous protuberance of the lateral surface

of the middle lobe reveals a mass of firmly clotted blood which completely fills the cavity. That portion of the lining of the cavity which lies against pulmonary tissue is unevenly mottled and streaked with yellowish patches, some of which contain calcific deposits. One of these atheroma-like plaques is slightly ulcerated. The opening of the artery is in the superior portion of the lateral wall of the cyst. The diameter of the artery as it enters the cavity is 7 by 5 mm. Near the hilum of the lung the artery reaches a maximal circumference of 23 mm. The lumen of the vein is larger than that of the artery. At its entrance into the aneurysmal sac it is approximately 1 cm. in diameter, and about 0.8 cm. in diameter near the hilum of the lung at the site of amputation. The intima of the artery shows very slight atheromatosis. That of the vein is essentially normal. The principal diameters of the aneurysmal sac are approximately 6.5 by 6.5 by 6 cm. At the hilum of the middle lobe the principal bronchus measures 0.8 cm. in diameter and its lumen is completely obstructed by a plug of inspissated mucus. The parenchyma in the ventral margin and in the inferior margin below the aneurysmal sac is indurated and apparently completely airless. It appears to have been greatly compressed by the cyst-like aneurysmal sac.

*Microscopic:* Section A—Taken through hilum of lung and including the artery: The wall of the artery shows no significant degree of degenerative disease until it reaches its expanded portion in the wall of the aneurysmal sac. On one side the smooth muscle wall continues as far as the area represented by the section but shows infiltrates of lymphocytes around the blood vessels of the adventitia and in the inner portion of the media. On the other side the muscular wall ends abruptly and is replaced by a wall of fibrous tissue with only occasional small bundles of smooth muscle. The large bronchus at the hilum is collapsed and its epithelium is missing from a large portion of the mucosa. No significant degree or inflammatory reaction is evident. The pulmonary parenchyma is partially atelectatic but otherwise not remarkable.

Section B—Elastic fiber stain of the same tissue: The arterial wall is composed almost entirely of collagenous tissue and smooth muscle. Only traces of elastic fibers are seen in the wall.

Section C—Section through the thin (lateral) portion of the aneurysmal sac: The wall contains smooth muscle and hyalinized fibrous tissue. The intima is unevenly thickened and in one place there is a calcified atheromatous plaque. Small bronchioles and alveoli are compressed against the wall of the sac.

Section D—In a section stained for elastic fibers no elastic tissue is found.

Sections E and F—Section through wall of aneurysm and pulmonary parenchyma of the medial side of the sac (hematoxylin and eosin and elastic fiber stains): The intima is unevenly thickened and elevated in the form of atheromatous plaques. In one area the media also appears to be degenerated and the collagenous fibers are separated. There is no ulceration and only one small focus of calcification is present in this section. The parenchyma which surrounds the sac is compressed and the air spaces are partly filled with edematous fluid and blood. Small foci of lymphocytic infiltration are located in the outer zone of the wall of the aneurysm.

*Diagnosis:* Arteriovenous "aneurysm" of the middle lobe of the right lung. Atheromatous degeneration with slight calcification of the wall of the aneurysm. Compression atelectasis, especially of the middle lobe of the lung.

## ANALYSIS OF CASES (INCLUDING PRESENT REPORT) (TABLE II)

*Sex.* Of the 27 cases, the sex was not mentioned in one. Fifteen were males and 11 females.

*Location.* In 5 instances the site of the tumor was not mentioned. In 5 cases the right lung and in 7 the left lung was involved. In 10 of the patients both lungs were involved with one or more vascular tumors.

## CLINICAL FINDINGS (TABLE II)

The analysis of the clinical findings is based on only 18 of the 27 cases. These were the only ones with sufficient clinical data to warrant inclusion and to distinguish them as an entity.

*Cyanosis.* Cyanosis was present in all of the 18 cases. Though a constant finding in this syndrome it varied in intensity from severe to minimal. In some patients it was noted as being transient, in others as constant.

TABLE II

CLINICAL FINDINGS

| Case No. | Authors | Sex | Age yr. | Cyanosis | Clubbing | Dyspnea | Vascular Anomalies | Bruit | Chest Pain | Hemoptysis | Enlarged Heart | Weakness | Dizziness | Faintness | Fatigue | Headache | Convulsions | Numbness | Epistaxis | Thick Speech |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 10 | Rodes 1938—autopsy | M | 25 | + | + | + | + | | + | + | o | | | + | | | + | | | |
| 11 | Smith and Horton 1939—angiogram | M | 40 | + | + | + | | + | + | | o | + | + | + | | | | + | | |
| 12 | Hepburn and Dauphinee 1942—pneumectomy | F | 23 | + | + | + | o | o | | | | | + | + | | | | | | + |
| 13 | Goldman 1943—clin. diag. | M | 22 | + | + | + | + | o | + | | o | + | | | | + | | | | |
| 14 | Janes 1943–44—resection | M | 30 | + | | | + | + | | + | | | | | + | | | | | |
| 15 | Jones and Thompson 1944—pneumectomy | F | 24 | + | + | | | + | | | o | | | | | | | | | |
| 16 | Adams *et al.* 1944—pneumectomy | M | 24 | + | + | | + | | | | o | | | | | | | | + | |
| 17 | Alexander 1945—autopsy | M | 41 | + | + | + | | + | | | + | | + | | | | | | | |
| 18 | Sisson *et al.* 1945—angiogram and autopsy | F | 45 | + | + | + | + | + | + | + | + | + | + | + | + | | + | + | | + |
| 19 | Lindgren 1946—clin. diag. | M | 30 | + | + | + | | + | + | | + | + | | | + | + | | | | |
| 20 | Lindgren 1946—lobectomy and angiogram | M | 29 | + | + | + | + | + | | + | o | | | | | | + | + | | |
| 21 | Lindgren 1946—lobectomy and angiogram | F | 25 | + | + | + | | + | | + | o | | | + | + | | | | | |
| 22 | Makler and Zion 1946—clinical | M | 20 | + | + | + | + | + | | | o | | | | | + | | | + | |
| 23 | Goldman 1947—pneumectomy | M | 22 | + | + | | | | | | | | | | | | | | | |
| 24 | Goldman 1947—no report | M | 32 | + | + | | | | | | | | | | | | | | | |
| 25 | Bierewaltes *et al.* 1947—lobectomy | F | 27 | + | + | + | + | | | | o | | | + | | | | + | + | |
| 26 | Burchell and Clagett 1947—pneumectomy | M | 20 | + | + | o | + | + | o | o | o | o | | o | o | | o | o | o | o |
| 27 | Crane *et al.* 1947—lobectomy | M | 45 | + | + | + | + | + | + | o | o | o | o | o | o | o | o | o | o | o |

*Dyspnea.* Dyspnea was recorded in 13 cases and not mentioned in 5. It was variable in its onset, constancy or degree of incapacity.

*Clubbing of Digits.* This was mentioned as being found in all cases except 2 in which no statement was made as to whether or not it was present. The degree of the clubbing could not be determined from the records. Both fingers and toes were involved. Its

disappearance after surgery was noted in 1 case. In another it was still present months after removal of the fistula.

*Bruit.* An audible bruit was present in 11 cases. It was definitely indicated as not being present in 2 cases. Its presence or absence was not mentioned in 5 cases. The phase during which the bruit was heard was inconstant.

*Visible Associated Vascular Anomalies.* This was recorded as being present in 9 instances and as not being present in 1 case. These consisted of external hemangiomas, varices and local telangiectasis. In 8 instances no reference was made.

*Chest Pain.* Chest pain was recorded as being present in 6 instances. It was usually sharp in nature, radiating and transient. In 11 cases it was not mentioned.

*Hemoptysis.* This was noted in 5 cases. (In Case 10 it was recorded as being fatal.) Small amounts of blood in the sputum was the most frequent manifestation. It was mentioned as definitely not being present in 1 instance. In 11 cases it was not mentioned at all.

*Cardiac Enlargement.* It was present in 3 cases. One of these (Case 17) died of coronary occlusion, a second had hypertension (Case 18) and a third (Case 19) had some form of clinical valvular disease. It was definitely recorded as not being present in 11 instances. In 3 cases there was no mention of the heart size. It is apparent that cardiac enlargement such as may occur with traumatic or congenital arteriovenous aneurysm of the peripheral circulation is not prominent in this syndrome.

*Lungs.* In 5 instances the records show that there was evidence of "consolidation" or dullness over the tumor site. Nine cases were reported as "clear."

*Weakness and Dizziness* were reported as being present in 5 cases.

*Fatigue* was prominent in 4 instances and *headache* was noted in 4 cases.

*Convulsions* occurred in 3 cases. In 1 case the patient had transient terminal convulsions (Case 18), in another (Case 20) it was noted that the patient had "some" convulsions, and the third (Case 10) had convulsions many years before the diagnosis of arteriovenous fistula was made.

*Transient numbness* was reported as occuring in 4 cases, at times related to body position.

*Epistaxis* was noted in 3 cases.

*Thick speech* was recorded in 2 instances.

### COMPOSITE CLINICAL PICTURE

The clinical picture is quite characteristic and could well be labelled a syndrome. The characteristic findings common to almost all of the cases were cyanosis, dyspnea, clubbing of the digits, and thoracic bruit. The associated findings of visible vascular anomalies, chest pain, hemoptysis, absence of cardiac enlargement, weakness, dizziness, faintness and fatigue occurred with sufficient frequency to warrant their inclusion in the syndrome.

### ROENTGEN FINDINGS (TABLE III)

In all 18 cases a definite statement was made of a tumor in the lung demonstrated roentgenologically. Rodes was the first to describe the roentgen findings in the lungs. The illustration in his paper is typical of an arteriovenous fistula. Smith and Horton were the first to achieve the angiographic demonstration of an arteriovenous fistula in the lung.

Multiple tumors were frequently noted. In Case 14 two were present in the right lung and one or possibly two in the left. Case 17 showed lesions in both the left and in the right lung field. Case 20 had a mass present in the right lung and two in the left. In Case 22 three shadows were present in the right and one in the left lung field.

In Case 10 the roentgenogram is not described. It is stated in the paper that there was a mass in the left lower lung field. Examination of the print in that article reveals the presence of a large, poorly delineated vascular shadow leading from the left hilum to a mass in the lung. This probably represents a dilated artery and

Table III

ROENTGEN AND PATHOLOGICAL FINDINGS

| Case No. | Location of Lesion | Pathological Findings | Roentgen Findings |
|---|---|---|---|
| 10 | Rt. posterior and lt. upper lobe | Multilocular multiple hemangiomas | Mass in the lt. lower lung field; dense bands to the hilum |
| 11 | Rt. base posteriorly | Probably arteriovenous fistula | Two dilated vessels arising in rt. hilum and communicating in parenchyma of rt. lung |
| 12 | Right lower lobe | Cavernous sinuses and cavernous angioma | Infiltration in the right middle and lower lobe |
| 13 | Left mid-lung field | Cavernous hemangioma | Pulsating mass |
| 14 | Rt. lower and middle lt. lower | Cavernous hemangioma | Two shadows in the rt. lung. One, possibly two, in the left |
| 15 | Right middle lobe | Varicosities over rt. upper lobe and A-V fistula | Mass in the rt. lower lung with a large vessel from the hilum |
| 16 | Three in left lung | Multilocular smooth lined cavities with A-V connections. Multiple A-V fistula | Moderately opaque areas |
| 17 | Lt. base, one large. Many small tumors in rt. and lt. lungs | Cavernous hemangioma. Direct connection with pulmonary vessels | Large round opacity at lt. base post. and a small one at rt. base. Vessels seen going to tumor |
| 18 | Both rt. and lt. lungs | Arteriovenous aneurysm | Round opaque area, well defined borders. No pulsation |
| 19 | Lt. interlobar fissure | A-V communication | Round density in lt. base. Broad density from it to hilum |
| 20 | Superior lobe on right | Hemangiomas | Irregular round formation in rt. interlobar septum. Two vessels lead to the hilum. Two similar shadows on lt. No pulsation |
| 21 | Lingula | Hemangioma | Irregular density connected to the hilum |
| 22 | Right and left | Pulmonary hemangioma | Opacities mid portion of rt. lung field. Vessels to the hilum |
| 23 | Lt. hilum lt. mid-lung field | Cavernous angioma | Mass in the left hilum and lt. lung |
| 24 | Left mid-lung | Pulmonary arteriovenous fistula | Mass in the left mid-lung |
| 25 | Left lower lobe | Pulmonary aneurysm | 3 cm. area with pulsation. A tail-like projection to hilum |
| 26 | Right middle lobe | No communication between the artery and vein. Varicose vessels with vascular sinuses | Irregular pulsating. Nodular shadow in right lung |
| 27 | Right middle lobe | Arteriovenous fistula | Opaque shadow in right mid-lung field |

vein leading to and from the arteriovenous fistula.

In Case 11 the roentgenogram was described as showing infiltration at the base of the right lung which was thought to be the result of bronchiectasis. Angiography demonstrated two dilated vessels communicating in the right lung. In Case 12 the roentgenogram was described as revealing an infiltrative process in the right middle and lower lobes which was shown by lipiodol injection not to be bronchiectatic. A second interpretation of other roentgenograms was given as "vascular endothelioma." The final diagnosis was noted as "pulmonary fibrosis." At a third examination it was felt that an abnormal arteriovenous communication on the order of a cavernous hemangioma was present.

In Case 13 the roentgenograms were

interpreted as showing a zone of homogenous opacity which had an intrinsic pulsation synchronous with the pulsation of the pulmonary artery as demonstrated by kymography.

In Case 14 the roentgenograms showed two shadows in the right lung and one in the left. The diagnosis rested between multiple hemangiomas and adenomas of the lung.

In Case 15 the roentgenoscopic examination was interpreted as showing the right hilum to be increased in density and containing a pulsating vessel radiating to a round mass 8 by 10 cm. in diameter. Body section roentgenograms demonstrated these to be vessels leading to a pulsating vascular mass in the lung. The vessels appeared to be composed of dilated branches of the pulmonary artery.

In Case 16 roentgenograms showed a lobulated moderately opaque area 25 cm. square and a second smaller area. The roentgen diagnosis was pulmonary fibrosis or arteriovenous shunt through an arteriovenous aneurysm or congenital heart disease.

In Case 17 the roentgenograms were interpreted as showing large rounded opacities at the left and right base. The diagnosis was emphysema and chronic bronchitis.

In Case 18 the roentgenograms showed a large opaque area in the left lung. Roentgenoscopically the mass did not pulsate. Bronchograms failed to reveal any communication with the bronchial tree. An angiogram with a catheter in the right auricle was reported to have been done. No other statement was added.

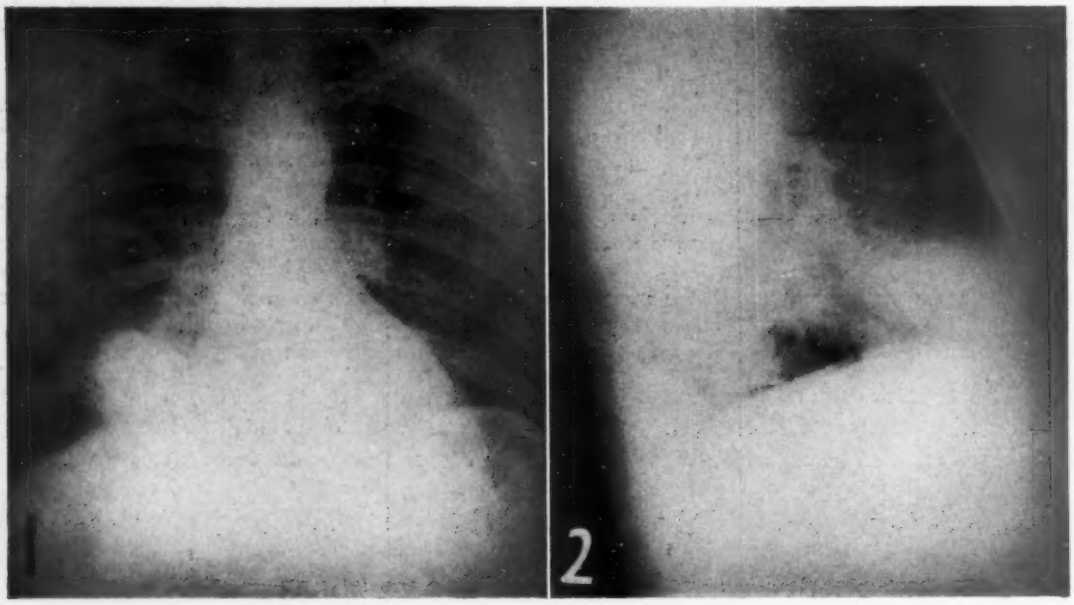


FIG. 1 and 2. Oval soft tissue tumor mass lying in region of right middle lobe. Right hilum extends lower than normal and communicates with soft tissue mass by two widened vascular shadows. Pulsation of vessels seen on roentgenoscopy.

In Case 19 an irregular rounded density was connected by broad sinuous densities to the vessels of the hilar region. It was diagnosed as an arteriovenous aneurysm. Roentgenoscopic examination failed to reveal any abnormal pulsations.

Case 20 showed the right lung to contain an irregular rounded formation connected with the hilum by a broad-shaped density of sinuous vessels. The left lung in this

same case showed two similar formations. Each of the rounded densities led to sinuous vessels that were wider than adjacent vessels and whose course deviated from other vessels. On the Valsalva test the volume of mass in the lung diminished. On the Müller test it increased. On roentgenoscopy the vessels did not pulsate. The diagnosis was arteriovenous aneurysm.

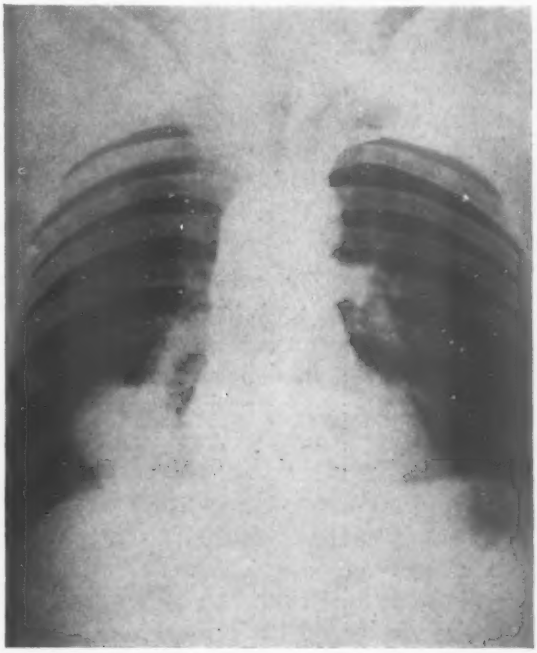

Fig. 3. Angiogram. Film taken two seconds after injection of diodrast. Tumor opacified. Vessel leading to it (artery) also opacified. Vein noted as fainter shadow.

In Case 21 there was an irregular density connected to the hilar region by broad-shaped densities which seemed to merge into the vessels of the latter. On the Valsalva and Müller tests there was respectively a decrease and an increase in size of the tumor shadow. On angiocardiography the contrast medium passed through the vessels and the densities became more dense. The diagnosis was arteriovenous aneurysm.

In Case 22 the description was that of a discrete opacity in the right lung and a less well defined irregular opacity in the left lung. From each of these opacities a broad linear shadow extended to the hilum. The patient was followed for a period of eight months during which no change appeared. Three years later, however, the patient was roentgenographed again and two new masses were noted in the lower right lung field. The Valsalva test showed a decrease and the Müller test showed an increase in the size of the masses. Pulsations could not be demonstrated roentgenoscopically. Laminagraphy showed the vessels to be dilated pulsating arteries. The lung field masses showed an irregular worm-like configuration. The diagnosis was multiple pulmonary hemangiomas.

Fig. 4. Angiogram. Film taken four seconds after injection. Tumor further opacified. Vessel to it (artery) less dense. Vessels in parenchyma of lung filled with opaque medium.

Case 23 showed in the roentgenogram a mass in the left hilum and left lung. Nothing is mentioned of vascular changes.

In Case 24 there was a mass in the left mid-lung.

Case 25 showed a 3 cm. area in the right lower lung field that pulsated. Leading from this to the hilum was a tail-like projection.

In Case 26 there was an irregular nodular

shadow in the right lung which pulsated during roentgenoscopic observation.

The case being reported (Case 27) showed a large soft tissue tumor mass which lay in the region of the right middle lobe (Fig. 1 and 2). Leading from the hilum to this mass were two large parallel vessels of different densities. The inferior vessel was much more dense than the superior one. During roentgenoscopic examination both vessels were noted to pulsate, the lower one more markedly than the upper. During the Valsalva test there was a definite decrease in the size of these vessels. During the Müller test they increased in size and density.

Angiocardiography demonstrated that these vessels and the tumor shadow communicated directly with the pulmonary vessels. As the opaque material left the main pulmonary artery the lower vessel and the tumor mass became markedly opacified (Fig. 3). As the tumor mass emptied of the opaque media the upper vessel and the smaller pulmonic vessels in the lung parenchyma became more visible due to increased opacification (Fig. 4). The diagnosis of an arteriovenous fistula was thus confirmed.

### COMPOSITE ROENTGEN FINDINGS

A review of the prints of the roentgenograms in the literature plus an analysis of the reports enables us to describe the characteristic roentgen appearance of an arteriovenous fistula in the lung.

This consists primarily of a round, smooth, soft tissue tumor mass usually in the lower lung field. The hilum of the involved side appears denser than the uninvolved one due to the added vascular bed. Arising from the hilum and converging on the soft tissue mass in the parenchyma, there are usually present two large sinuous blood vessels. One of these will show definite pulsations synchronous with the pulmonary artery. This probably represents a pulmonic artery. The other, the vein, will show minimal to no pulsation. The pulsation may be demonstrated on roentgenoscopy or a permanent record obtained by kymography. The vascular nature of the tumor mass can be demonstrated by means of angiography. This technique lends itself admirably to the visualization of the normal pulmonary circulation and any aberrations present. The independent filling of the pulmonary arterial and venous systems can be demonstrated by taking serial films. The phase of opacification of the vessels leading to the tumor mass indicates which is the artery and which is the vein. Opacification of the tumor mass itself labels it as a vascular lesion.

There are other valuable maneuvers which can be used to substantiate the diagnosis. The Valsalva test in which increased intrathoracic pressure prevents the flow of blood into the pulmonary bed causes the vascular tumor and its vessels to decrease in size. In the opposite or Müller test in which the intrathoracic pressure is decreased and a negative force exerted, the tumor and its vessels increase in size. Catheterization of the heart and the right pulmonary vein with analysis of blood samples for oxygen content should also offer diagnostic data. Procedures of negative value such as bronchoscopy. bronchography and pneumothorax, may be used to demonstrate that the tumor mass is not related to the bronchial tree.

### LABORATORY DATA—TABLE IV—(GROUP OF EIGHTEEN CASES)

*Hemoglobin.* The values are given in some instances as grams of hemoglobin or percentage of normal or as in Case 14 as "normal" without any figure. In Case 21 no mention was made of the hemoglobin value. Of the cases in which reports are available all showed an increase in hemoglobin ranging between 108 per cent (Case 10) and 138 per cent (Case 13) hemoglobin, or 19.5 grams (Case 22) and 32.7 grams of hemoglobin (Case 11).

Several cases show variation in the hemoglobin values which should be noted. Case 14 was reported as normal. The patient, as expected, had no clinical findings which

could be correlated with decreased blood oxygenation. Case 19 was recorded as having 55 per cent of hemoglobin for which there is no explanation. Case 18 was recorded as having 14.5 grams of hemoglobin. This patient had both acute renal and cardiac disease as well as multiple episodes of hemoptysis any of which could have produced the anemia.

*Red Blood Cell Counts.* The counts ranged between a maximum value of 11.45 million (Case 13) and 6.2 million red blood cells per cubic centimeter (Case 23). The case with 55 per cent hemoglobin (Case 19) had a red blood count of 4.3 million. Case 18 with 14.5 grams of hemoglobin did not have a red blood count recorded. In Case 21 the red blood count was not mentioned. Case 14 was recorded as having a normal count with microcytosis and hypochromia.

*Hematocrit.* The hematocrit was recorded in only 8 cases. The values ranged from 82 preoperative in Case 24 to 64 in Case 26. Following surgery there was a rapid return to normal.

*White Blood Cell Count.* The white blood cell count was in no instance significantly elevated. This is an important differential point inasmuch as in true polycythemia there is a leukocytosis. In 4 cases the count was not recorded. Two cases were reported as having counts of 3,200 (Case 11) and 4,700 (Case 13). In the remaining cases the values ranged between 6,500 and 11,400.

TABLE IV

LABORATORY DATA

| Case No. | Author | Hemoglobin | R.B.C. | Hematocrit | W.B.C. | Platelets | Blood Volume cc. | Plasma Volume cc. | Volume of Cells cc. |
|---|---|---|---|---|---|---|---|---|---|
| 10 | Rodes | 108%<br>118% | 7.54 | | 9,800<br>10,700 | | | | |
| 11 | Smith and Horton | 20.6 gm.<br>32.7 gm. | 6.47 | 66 | 3,200<br>7,300 | 104,000 | 6,068 | 760 | |
| 12 | Hepburn and Dauphinee | 12.2 gm.<br>21.8 gm. | 9.6 | 80 | | | 8,500<br>3,500 | | |
| 13 | Goldman | 137% | 11.45 | | 4,100 | 855,000 | 8,170 | 2,450 | 5,720 |
| 14 | Janes | Marked microcytosis and hypochromia | | | 11,400 | | | | |
| 15 | Jones and Thompson | 130% | 6.5<br>7.5 | | 7,350 | Normal | | | |
| 16 | Adams, Thornton and Eichelberger | 23 gm. | 7.2 | | 6,600 | | 12,750 | 2,420 | 10,330 |
| | Postoperative | 17.0 gm. | 4.94 | 63 | 12,300 | | 4,970 | 2,280 | 2,690 |
| | | | 6.04 | | 7,000 | | 6,900 | 2,920 | 4,350 |
| 17 | Alexander | 20.4 gm. | 8.2 | | 5,100 | | | | |
| | | | 2.5 | | 7,600 | | | | |
| 18 | Sisson *et al.* | 14.5 gm. | | | 9,120 | | | | |
| 19 | Lindgren | 55% | 4.3 | | | | | | |
| 20 | Lindgren | 125% | 6.48 | | | | | | |
| 21 | Lindgren | | | | | 175,000 | | | |
| 22 | Makler and Zion | 19.5 gm. | 7.7 | 55 | 6,500 | | | | |
| 23 | Goldman | | 11 | | | | | | |
| 24 | Goldman | | 7 | | | | | | |
| 25 | Beierwaltes and Byron | 21.6 gm. | 8.2 | 75 | | 7,000 | | | |
| 26 | Burchell and Clagett | 24.1 gm. | 7.59 | 82 | | | 11,716 | 2,516 | 9,180 |
| 27 | Crane, Lerner and Lawrence | 19.5 gm. | 6.2 | 64 | 6,200 | | | | |
| | Postoperative | 15.9 gm. | 5.59 | 50 | 7,500 | | 5,535 | 3,010 | |

TABLE V

BLOOD OXYGEN VALUES

| Case No. | Oxygen Capacity | | Oxygen Content | | Per Cent Saturation | | Venous Oxygen Content | |
|---|---|---|---|---|---|---|---|---|
| | Pre-operative | Post-operative | Pre-operative | Post-operative | Pre-operative | Post-operative | Pre-operative | Post-operative |
| 12 | | | | | 70–75 | | | |
| 13 | 27.4 | | 16.7 | | 70 | | 9.5 | |
| 16 | 35.54 | 20<br>24.7 | 25.1 | 17.87 | 71 | 72.95 | 22.5<br>(63% unsat.) | 14.8<br>(14–33% unsat.) |
| 19 | 13.8 | | 12.5 | | 89.9 | | | |
| 25 | | | | | 77 | 92.2 | | |
| 26 | 30.8 | 14.8<br>(15 days)<br>20.2<br>(10 wk.) | 22.8 | 13.7<br>(15 days)<br>19.0<br>(10 wk.) | 74 | 92<br>(15 days)<br>98<br>(10 wk.) | | |
| 27 | 25.54 | 19.42 | 23.07 | 17.7 | 90.3<br>(normal is 95%) | 91.1 | 9.98 | |

*Platelets.* In the 4 cases in which there is a record the values were recorded as 104,000 (Case 11), 855,000 (Case 13), 175,000 (Case 21), normal (Case 15).

*Blood Oxygen Values.* These were only reported in a few cases (see Table v).

*Incidental Reports.* Circulation time, electrocardiographic findings, vital capacity, pulse rate and blood pressure were all normal.

## DISCUSSION

The presence of an arteriovenous fistula provides a shunt in the lung so that a portion of the blood is unoxygenated. This produces a demand for increased red blood cell production, i.e. a secondary polycythemia. The mechanism of the erythrocytosis is assumed to be the low oxygen saturation of the arterial blood, either acting directly on the bone marrow or by way of some by-product of asphyxia. In the absence of erythrocytosis evidence of anoxia may occur in the form of cyanosis, dyspnea and syncope. In contrast to polycythemia vera the white blood cell count is not elevated nor is the spleen enlarged. The typical syndrome of cyanosis, dyspnea, clubbing of the digits, plus a bruit, associated with secondary polycythemia due to an arteriovenous shunt in the lung can easily be mistaken for congenital heart disease.

The increasing number of reports in the literature of arteriovenous fistulas of the lung indicates that this entity has in the past been overlooked. The excellent results achieved by the thoracic surgeon in the correction of this condition now affords these patients a chance for normal living.

## SUMMARY

A case of an arteriovenous fistula of the lung is reported. The characteristic clinical. laboratory and roentgen findings based on an analysis of the available literature are noted.

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314 Commonwealth Ave.
Boston, Mass.

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# THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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*Thirty-second Annual Meeting:* 1950, to be announced.

# EDITORIALS

## MINERAL OIL PNEUMONITIS

DURING routine photofluorographic examinations of the chest not infrequently obscure lesions of the lungs are encountered which constitute a challenge to the diagnostic ingenuity of the investigator. Perhaps the most interesting of these lesions is a silent circumscribed shadow accidentally discovered in one of the lower lobes of a healthy appearing elderly person. Although the roentgen findings are not altogether typical and bronchoscopic biopsy proves negative for malignancy, usually a clinical diagnosis of cancer of the lung is made and lobectomy or pneumonectomy recommended. Then at operation, surprisingly, a pneumonitis is found.

Schneider[1] recently called attention to the fact that the habitual use of mineral oil for constipation has a very definite role in the production of such lesions. During a tuberculosis case-finding survey of two years he picked up seven cases of pneumonitis which were due to taking of liquid petrolatum as a laxative for many years. Based on these cases and by reviewing the literature dealing with oil aspiration pneumonitis, he established the salient features which characterize this disease.

The ingested mineral oil enters the lungs through overspilling into the larynx. Schneider found that in most cases this overspilling is due to absence or diminution of the gag reflex. However, the liquid petrolatum is so bland that, especially in older persons, it may pass from the nasopharynx into the larynx even when the neurologic examination is entirely negative. The repeated deposition of very small quantities of the oil in the lower bronchi provokes, after a considerable period of time, a persisting local reaction eventually leading to a demonstrable opacity in the roentgenograms. Once the pneumonitis has appeared, it will continue to slowly advance as long as the patient takes the oil laxative.

It has been known for some time that in patients with defective swallowing, whether due to an interfering organic lesion, or a nervous dysphagia or simply to extreme debility, mineral oil as a habitual laxative leads not infrequently to lipid pneumonitis. There are several reports published from large institutions caring for the mentally ill, aged and chronically sick emphasizing this fact and cautioning against the administration of oil laxatives in such patients. Likewise, the danger of producing aspiration pneumonitis from oil medication in nose and throat conditions, especially in children, has been repeatedly stressed. Other authors described the harmful effect that may result in the lungs from the prolonged use of oily nose drops or oily nasal sprays. What makes Schneider's observation of particular interest is the fact that he now reports that oil aspiration pneumonitis also occurs in apparently healthy persons addicted to the habitual use of mineral oil who exhibit very few or no clinical symptoms.

A study of the pathogenesis of lipid pneumonitis shows that various oils act in a different manner. Saponifiable animal oils which contain large amounts of fatty acids (or lead, when in contact with the tissue enzymes, to formation of fatty acids) produce severe immediate reactions upon entering the lungs. The saponifiable vegetable oils commonly used as vehicles for other drugs or as the carriers of opaque media produce no immediate reaction but may lead to pulmonary changes after a very prolonged use. The liquid petrolatum, or mineral oil, is a non-saponifiable oil and

[1] Schneider, Louis. Pulmonary hazard of the ingestion of mineral oil in the apparently healthy adult. *New England J. Med.*, 1940, *240*, 284–291.

therefore behaves as an inert foreign body. After repeated aspirations the accumulation of the oil in the alveoli of the lungs sets in motion a process which is dominated by phagocytic phenomena first and by fibrotic changes later.

The distribution of mineral oil pneumonitis follows the law of gravity of the descending free fluid. Since most patients are ambulatory adults, the most frequent site of involvement is the base of the right lung. Occasionally the lesion may be located in the base of the left lung and in the long protracted cases, as a rule, both sides become affected.

Clinically, the most striking features of mineral oil pneumonitis are the paucity of symptoms and the disproportion between the remarkably good general condition of the patient and the advanced degree of pulmonary involvement. All the cases of Schneider were discovered accidentally. Sometimes the examined person complained of a slight dry hacking cough and of some shortness of breath on exertion, but at an advanced age such symptoms could easily be attributed to arteriosclerotic heart disease.

Regarding the roentgen appearance of mineral oil pneumonitis, Schneider states that in the earliest cases no localized findings or only increased markings in the affected area may be present. Later, a small, circumscribed opacity is found, usually resembling a bronchopneumonic focus. When marked proliferative reaction constitutes part of the histopathologic process the opacity may appear quite dense, giving an image not unlike that observed in primary carcinoma of the lung. With further advance of the lesion, the bronchopneumonic infiltrations may fuse into "an ill defined area of ground-glass density" and the involvement may become bilateral. Not infrequently, recurring acute pneumonitis may be superimposed on the very slowly progressing chronic process.

The diagnosis of mineral oil pneumonitis, if all the facts are known, is relatively simple. A differentiation from basal tuberculosis, primary bronchiectasis and mycotic infections, as a rule, encounters no difficulty. The unilateral solitary form may erroneously be diagnosed as primary carcinoma of the lung. However, the peripheral extension, the absence of pressure atelectasis and the lack of metastatic involvement of the hilar glands are valuable signs supporting the diagnosis of mineral oil pneumonitis.

Schneider also stresses the importance of two confirmatory tests. One of these consists in the examination of the sputum for oil droplets. The patient is asked to discontinue taking mineral oil and after several days the morning sputum is collected for three successive days in a wide-mouthed jar which is kept in a refrigerator. By placing cigarette paper or a piece of lens paper on the surface of the accumulated sputum, grease spots will appear on the thin paper. As further proof the sputum is stained. The mineral oil droplets will take the characteristic stain with scarlet red, whereas the saponifiable fats and oils take the stain with osmic acid. The second confirmatory test is an aspiration biopsy of the affected portion of the lung which is then stained with scarlet red.

The treatment of mineral oil pneumonitis is started by advising the patient to discontinue taking mineral oil. The early changes may clear up spontaneously or may regress to a point where no further intervention is necessary. When superimposed infection or bronchiectasis complicates the picture lobectomy may be indicated.

All in all, it appears that by taking into consideration the above enumerated factors, a larger number of cases of mineral oil pneumonitis will be discovered during routine chest surveys. By properly differentiating this benign disease from primary carcinoma of the lung, some needless radical operations may be avoided. The recognition of the possible pulmonary hazard of mineral oil may also lead to prescribing of some other types of habitual laxatives for old people.

T. LEUCUTIA, M.D.

# ANDERS PETER OVERGAARD
## 1879-1948

DR. ANDERS PETER OVERGAARD, Houston, Texas, radiologist, died on March 14, 1948. A native of Kennard, Nebraska, Dr. Overgaard was born March 4, 1879, the son of Anders C. and Dorthea Overgaard. He attended Kennard High School and the University of Nebraska College of Medicine, Omaha, from which he was graduated in 1900. He served an internship at Paxton Douglas County Hospital, Omaha, and then practiced for fourteen years at Freemont and twenty-four years at Omaha before moving to Houston in 1940. He retired from active practice in 1947.

Since coming to Texas Dr. Overgaard

had been a member of the Harris County Medical Society, the State Medical Association, and the American Medical Association. He was a member of the South Texas District Medical Society and the Houston Academy of Medicine. He was an honorary member of the Harris County Medical Society and had been nominated for honorary membership in the State Medical Association at the time of his death. He was a diplomate of the American Board of Radiology, a charter member of the American College of Radiology, and a member of the American Roentgen Ray Society and Radiological Society of North America. While in Nebraska, Dr. Overgaard had served as president of the Omaha Roentgen Society and Omaha-Douglas County Medical Society and as a councilor of the Nebraska State Medical Association. He was a member of the Episcopal Church, the Masonic Order, and the Shrine.

Dr. Overgaard is survived by his wife, the former Miss Gertrude Fleming of Freemont, Nebraska, whom he married in 1905.

C. P. HARRIS, M.D.

# SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

## MEETINGS OF ROENTGEN SOCIETIES*

### United States of America

**American Roentgen Ray Society**
*Secretary*, Dr. H. Dabney Kerr, University Hospital, Iowa City, Iowa. Annual meeting: Netherland Plaza Hotel, Cincinnati, Ohio, Oct. 4–7, 1949.

**American Radium Society**
*Secretary*, Dr. H. F. Hare, 605 Commonwealth Ave., Boston, Mass. Annual meeting: 1950, to be announced.

**Radiological Society of North America**
*Secretary*, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Cleveland Auditorium and Statler Hotel, Cleveland, Ohio, Dec. 4–9, 1949.

**American College of Radiology**
*Executive Secretary*, William C. Stronach, 20 N. Wacker Drive, Chicago 6. Annual meeting: 1950, to be announced.

**Section on Radiology, American Medical Association**
*Secretary*, Dr. Paul C. Hodges, 950 E. 59th St., Chicago, Ill. Annual Meeting: 1950, to be announced.

**Alabama Radiological Society**
*Secretary*, Dr. W. W. Anderson, Tuscaloosa, Ala. Meets time and place Alabama State Medical Association.

**Arizona Association of Pathologists and Radiologists**
*Secretary*, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

**Arkansas Radiological Society**
*Secretary*, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

**Atlanta Radiological Society**
*Secretary*, D. W. W. Bryan, 490 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

**Brooklyn Roentgen Ray Society**
*Secretary*, Dr. J. J. Daversa, 345 75th St., Brooklyn, N. Y. Meets monthly fourth Tuesday, Oct. through April.

**Buffalo Radiological Society**
*Secretary*, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

**Central New York Roentgen Ray Society**
*Secretary*, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

**Central Ohio Radiological Society**
*Secretary*, Dr. Paul D. Meyer, Grant Hospital, Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Seneca Hotel, Columbus, Ohio.

**Chicago Roentgen Society**
*Secretary*, Dr. John H. Gilmore, 720 N. Michigan Ave., Chicago 11, Ill. Meets second Thursday of each month October to April inclusive at the Palmer House.

**Cincinnati Radiological Society**
*Secretary*, Dr. Eugene L. Saenger, 735 Doctors Bldg., Cincinnati 2, Ohio. Meets last Monday of each month, September to May, inclusive.

**Cleveland Radiological Society**
*Secretary*, Dr. J. R. Hannan, Cleveland Clinic, Cleveland 6, Ohio. Meetings at 6:30 P.M. on fourth Monday of each month from October to April.

**Colorado Radiological Society**
*Secretary*, Dr. Mark S. Donovan, 306 Majestic Bldg., Denver 2, Colo. Meets third Friday of each month at Department of Radiology, Colorado School of Medicine.

**Connecticut Valley Radiologic Society**
*Secretary*, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday Oct. and April.

**Dallas-Fort Worth Roentgen Study Club**
*Secretary*, Dr. X. R. Hyde, Medical Arts Bldg., Fort Worth, Texas. Meets in Dallas on odd months and in Fort Worth on even months, on third Monday, 7:30 P.M.

**Detroit Roentgen Ray and Radium Society**
*Secretary*, Dr. W. G. Belanger, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

**East Bay Roentgen Society**
*Secretary*, Dr. Dan Tucker, 434-30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

**Florida Radiological Society**
*Secretary*, Dr. F. K. Hurt, Riverside Hospital, Jacksonville, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

**Georgia Radiological Society**
*Secretary*, Dr. Robert Drane, DeRenne Apartments, Savannah, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

**Houston X-ray Club**
*Secretary*, Dr. Curtis H. Burge, 3020 San Jacinto St. Houston 4, Texas. Meets fourth Monday each month.

**Radiological Society of Kansas City**
*Secretary*, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

**Illinois Radiological Society**
*Secretary*, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

**Indiana Roentgen Society**
*Secretary*, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

**Iowa X-Ray Club**
*Secretary*, Dr. Arthur W. Erskine, 326 Higley Bldg., Cedar Rapids, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. Special meetings by announcement.

**Kansas Radiological Society**
*Secretary*, Dr. Anthony F. Rossitto, Wichita Hospital, Wichita, Kan. Meets annually with State Medical Society.

**Kentucky Radiological Society**
*Secretary*, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in Apr.

**Kings County Radiological Society**
*Secretary*, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

**Los Angeles Radiological Society**
*Secretary*, Dr. Wybren Hiemstra, 1414 S. Hope St., Los Angeles 15, Calif. Meets second Wednesday each month at Los Angeles County Medical Assn. Building.

**Louisiana Radiological Society**
*Secretary*, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society Meeting.

**Louisville Radiological Society**
*Secretary*, Dr. E. L. Pirkey, Louisville General Hospital, Louisville 2, Ky. Meets monthly on second Friday at Louisville General Hospital.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
*Secretary*, Dr. R. D. McDuff, 220 Genesee Bank Bldg., Flint 3, Mich.

MILWAUKEE ROENTGEN RAY SOCIETY
*Secretary*, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
*Secretary*, Dr. Chauncey N. Borman, 802 Medical Arts Bldg., Minneapolis 2, Minn. Two meetings yearly, one at time of Minnesota State Medical Association the other in the fall.

NEBRASKA RADIOLOGICAL SOCIETY
*Secretary*, Dr. Ralph C. Moore, Nebraska Methodist Hospital, Omaha 3, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
*Secretary*, Dr. George Levene, Massachusetts Memorial Hospitals, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
*Secretary*, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
*Secretary*, Dr. F. H. Ghiselin, 111 East 76th St., New York 21, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. E. Hemphill, 1420 E. Fifth St., Charlotte 4, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
*Secretary*, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings held by announcement.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB
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OKLAHOMA STATE RADIOLOGICAL SOCIETY
*Secretary*, Dr. W. E. Brown, Tulsa, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
*Secretary*, Dr. Boyd Isenhart, 214 Medical Dental Bldg., Portland 5, Oregon. Meets monthly 2nd Wednesday, 8:00 P.M., Library of University of Oregon Medical School.

ORLEANS PARISH RADIOLOGICAL SOCIETY
*Secretary*, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
*Secretary*, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
*Secretary*, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. M. Converse, 416 Pine St., Williamsport. Annual Meeting: May 20 and 21, 1949, Bedford Springs Hotel, Bedford, Pa.

PHILADELPHIA ROENTGEN RAY SOCIETY
*Secretary*, Dr. G. P. Keefer, 1930 Chestnut St. Meets first Thursday each month October to May, at 8:00 P.M., in Thomson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
*Secretary*, Dr. R. P. Meader, 4002 Jenkins Arcade Pittsburgh 22, Pa. Meets 6:30 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

QUEENS ROENTGEN RAY SOCIETY
*Secretary*, Dr. J. E. Goldstein, 88-29 163rd St., Jamaica 3, N. Y. Meets fourth Monday of each month except during the summer.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
*Secretary*, Dr. Harry A. Miller, 2452 Eutaw Place, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
*Secretary*, Dr. Fred Zaff, 135 Whitney Ave., New Haven, Conn. Meets bimonthly on second Wednesday.

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY
*Secretary*, Dr. K. C. Corley, 1835 Eye St., N. W., Washington, D. C. Meets Medical Society Auditorium, third Thursday, January, March, May, October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
*Secretary*, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF NEW JERSEY
*Secretary*, Dr. Raphael Pomeranz, 31 Lincoln Park, Newark, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
*Secretary*, Dr. Ralph E. Alexander, 101 Medical Arts Bldg. Meets monthly on third Monday from October to May, inclusive, 8 P.M. at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
*Secretary*, Dr. Maurice D. Frazer, 1037 Stuart Bldg., Lincoln, Nebr. Meets Shirley-Savoy Hotel, Denver, Colo. August 18, 19, 20, 1949.

ST. LOUIS SOCIETY OF RADIOLOGISTS
*Secretary*, Dr. C. J. Nolan, 737 University Club Bldg., St. Louis 3, Mo. Meets fourth Wednesday each month, except June, July, August, and September.

SAN DIEGO ROENTGEN SOCIETY
*Secretary*, Dr. R. F. Niehaus, 1831 Fourth Ave., San Diego, Calif. Meets monthly, first Wednesday at dinner.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
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SHREVEPORT RADIOLOGICAL CLUB
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SOUTH CAROLINA X-RAY SOCIETY
*Secretary*, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
*Secretary*, Dr. J. M. Frère, 707 Walnut St., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

TEXAS RADIOLOGICAL SOCIETY
*Secretary*, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas. Next meeting, Dallas, Texas, February 3 and 4, 1950.

UNIVERSITY OF MICHIGAN DEPARTMENT OF ROENTGENOLOGY STAFF MEETING
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE
*Secretary*, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May inclusive. Room 203, Service Memorial Institute, 426 N. Charter St., Madison.

Utah State Radiological Society
*Secretary*, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets third Wednesday in September, November, January, March and May.

Virginia Radiological Society
*Secretary*, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
*Secretary*, Dr. Homer V. Hartzell, 310 Stimson Bldg., Seattle 1, Wash. Meets fourth Monday each month, October through May, College Club, Seattle.

X-Ray Study Club of San Francisco
*Secretary*, Dr. W. F. Reynolds, University of California Hospital, San Francisco. Meets from January to July, 1949, at Lane Hall, Stanford University Hospital, and from July to December 1949, at San Francisco Hospital.

### Cuba

Sociedad de Radiología y Fisioterapia de Cuba
*President*, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

### Mexico

Sociedad Mexicana de Radiologia y Fisioterapia
*General Secretary*, Dr. D. P. Cossio, Marsella No. 11, Mexico, D. F. Meets first Monday of each month.

### British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 p.m.
Medical Members' meeting, on third Friday in each month at 5:00 p.m., 32 Welbeck St., London, W 1.

Faculty of Radiologists
*Honorary Secretary*, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 p.m. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
*Honorary Secretary*, Dr. E. M. Crawford, 1535 Sherbrooke St., West, Montreal 26, Que. Meetings January and June.

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Western Australia, Dr. A. M. Nelson, 179-B St. Georges Terrace, Perth.
New Zealand, Dr. E. G. Lynch, 12 Bolton St., Wellington.

### South America

Sociedad Argentina de Radiologia
*Secretary*, Dr. Guido Gotta, Buenos Aires, Argentina. Meetings are held monthly.

Sociedad Argentina de Radiología, Filial del Litoral
*President*, Dr. Francisco P. Cifarelli. Meets second Wednesday each month, at 7:00 p.m., at 663 Italia St. in Rosario.

Sociedade Brasileira de Radiologia Medica
*Secretary*, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
*Secretary*, Dr. Andrelino Amaral, Av. Brigadeiro Luiz Antonio, 644, São Paulo, Brazil. Meets monthly on second Tuesday at 9 p.m. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Peruana de Radiologia
*Secretary*, Dr. Julio Bedoya Paredes, Apartado, 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
*Secretary*, Dr. Arias Bellini.

### Continental Europe

Société Belge de Radiologie
*General Secretary*, Dr. S. Masy, 111 Avenue des Alliés, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Ceskoslovenská společnost pro röntgenologii a radiologii v Praze
*Secretary*, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Polish Society of Radiology
*Secretary*, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Next meeting, Krakow, June 2 and 3, 1949.

Gdansk Section, Polish Society of Radiology
*Secretary*, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10.30, X-Ray Dept., Akademia Gdansk.

Warsaw Section, Polish Society of Radiology
*Secretary*, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland. Meets monthly.

Societatea Romana de Radiologie si Electrologie
*Secretary*, Dr. Oscar Meller, Str. Banual Măräcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad. USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
*Secretaries*, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
*Secretaries*, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock, State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
*Secretaries*, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 p.m.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
*Secretary*, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
*President*, Dr. H. E. Walther, Gloriastr. 14, Zürich, Switzerland.

Societa Italiana di Radiologia Medica
*Secretary*, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

## DISTRIBUTION PROGRAM FOR CYCLOTRON-PRODUCED RADIOISOTOPES

Cyclotron-produced radioisotopes will be made available to research men in the United States under a program announced July 23, 1949, by the Atomic Energy Commission. With this additional supply of radioisotopes which are produced in the accelerator type of atom-smashing machines added to the varieties produced in the Oak Ridge reactor, researchers will have a new collection of tools for finding answers to problems in general science, medicine, industry, and agriculture.

The program will augment the present distribution of reactor-produced radioisotopes which has been in effect since August, 1946. Up to the present, 6,975 shipments of radioisotopes of nearly 60 elements representing nearly 100 isotopic species have been made for research purposes through the facilities of the Atomic Energy Commission.

Only those cyclotron-produced isotopes having half-lives of more than 30 days will be distributed initially. Included in these are 43-day beryllium 7, 3-year sodium 22, 44-day iron 59, 4-year iron 55, 250-day zinc 65, 90-day arsenic 63, and 56-day iodine 125. Other cyclotron-produced radioisotopes of significant value as tools of research may be added at a later date.

The new program was strongly recommended by the National Research Council, which stated that "there are significant numbers of radioisotopes which either cannot be produced by the uranium chain-reacting pile or cannot be so prepared as to meet certain requirements that are obligatory for many scientific applications." The National Research Council also pointed out that the great number of requests for cyclotron-produced isotopes make it impossible for any one cyclotron laboratory to satisfy the demand without seriously interfering with its research programs.

Processing of irradiated targets will be carried out by the Oak Ridge National Laboratory in facilities already provided for handling reactor-produced isotopes. The Isotopes Division of the Commission will carry out the allocation function in the same manner as it now does with reactor-produced isotopes.

Cyclotron-produced radioisotopes, because of the method of their manufacture, are considerably more expensive than reactor-produced isotopes and in order to price them at a level which will make them available to most research institutions it will be necessary for the Commission to subsidize the program to a certain extent. In addition, these isotopes, like the reactor-produced radioisotopes now distributed by the Commission, also will be made available free of all production charges for cancer research.

Including distribution of cyclotron-produced isotopes in the present program for supplying reactor-produced radioactive isotopes will simplify maintenance of present policies on health safety requirements, disposal procedures, and criteria for use in human beings.

The distribution of materials produced under this program will be limited to institutions and organizations within the United States and its territories and possessions. Cyclotron-produced isotopes are more readily available abroad than reactor-produced isotopes because cyclotrons are in operation in many countries.

## UNITED NATIONS EDUCATIONAL, SCIENTIFIC AND CULTURAL ORGANIZATION

The United Nations Educational, Scientific and Cultural Organization (Unesco) proposes to publish later in the year a Manual on the International Exchange of Publications.

It is intended to publish as an annex to this Manual a classified list of institutions, including libraries, universities, scientific institutions, learned societies, etc. throughout the world, which are willing to exchange either their own publications or other publications which they have regularly at their disposal. In the course of its

activities Unesco has been able to obtain a considerable amount of information concerning the availability of exchange material, but the information at their disposal is still far from complete. All institutions which have so far not sent to Unesco details of their exchange material in one form or another are therefore urged immediately to communicate the following information to the Unesco Clearing House for Publications, 19 Avenue Kleber, Paris 16e, France:

(a) Name and full address of institution.

(b) Exact titles of publications offered. (In the case of duplicates offered for exchange purposes actual lists of duplicates are not required, but only a statement that lists of duplicates are available. Institutions possessing a catalogue of their own publications available for exchange are asked only to send a copy of the catalogue or to give a full bibliographical description of the catalogue.)

(c) Institutions which wish to exchange their publications only under certain conditions are asked to state what these conditions are.

Only information which reaches Unesco before October 1, 1949, can be used in the Manual and it is therefore in the interests of all institutions concerned to communicate immediately with the above address.

## CONTINUATION COURSE IN PEDIATRIC ROENTGENOLOGY

The University of Minnesota announces a continuation course in Pediatric Roentgenology on October 31 through November 5, 1949. The course, which will be presented at the Center for Continuation Study, is intended for radiologists and pediatricians. The material to be presented will include the basic medical sciences, clinical medicine, and diagnostic roentgenology, as it pertains to general and special problems in the field of childhood diseases. Presentation will be by means of lectures, clinics, conferences, and round table discussions.

Distinguished visiting physicians who will participate as members of the faculty for the course will include Dr. John Caffey, Babies Hospital, Columbia University Medical Center; Dr. Edward B. D. Neuhauser, Children's Hospital, Boston; Dr. Edith Potter, University of Chicago; and Dr. Frederic N. Silverman, Children's Hospital, Cincinnati. The remainder of the faculty for the course will be made up of clinical and full-time members of the staff of the University of Minnesota Medical School and the Mayo Foundation.

## CORRECTION

A paper by Bernard Roswit and Gustave Kaplan entitled "The Role of Nitrogen Mustard (HN2) as a Systemic Adjunct to the Radiation Therapy of Certain Malignant Diseases" appeared in this JOURNAL, May, 1949, Vol. 61, pp. 626–636. In the last paragraph on page 632 is this statement:

"*Bronchogenic Carcinoma.* In the Radiation Clinic more than 6,000 cases of inoperable bronchogenic carcinoma have received palliative deep roentgen therapy in the past fifteen years."

This contains an error as to the number of cases and it should read as follows:

"*Bronchogenic Carcinoma.* In the Radiation Clinic more than 600 cases of inoperable bronchogenic carcinoma have received palliative deep roentgen therapy in the past fifteen years."

## CORRECTION

In my abstract of the article "Late Results of Radium Therapy for Carcinoma of the Uterine Cervix," *J.A.M.A.*, July 10, 1948, *137*, 935–942, published in this JOURNAL in June, 1949, *61*, p. 878, in next to the last paragraph on that page I have listed the percentage followed up as "(varying from 25 per cent to 43.6 per cent)." These figures actually represent variation in the percentage of five year survival of traced patients according to age group. The percentage of those traced out of the total number actually approximates 90 per cent.

WILLIAM E. HOWES, M.D

# ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

*Department Editor:* GEORGE M. WYATT, M.D., 1835 Eye St., N.W., Washington 6, D. C.

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## ROENTGEN DIAGNOSIS

### NECK AND CHEST

Greenfield, Maurice M. Malignant plasmocytoma of the naso-pharynx: *Radiology*, May, 1948, *50*, 661–665.

A case history is presented of a twenty year old male with a right cervical adenopathy and small areas of destruction of the sixth rib on both sides. Biopsy revealed plasmocytoma for which he received intensive irradiation. One and one-half years later, he complained of nasal obstruction and right orbital headaches. Polypoid growths were removed from the nose in 1943 and had now recurred. Biopsy revealed plasmocytoma and roentgenograms showed bone destruction in the region of the right orbit. The case is presented to show the malignant character of plasmocytoma and its semiresistance to irradiation.—*C. H. Warfield, M.D.*

Black, Marden. Surgical aspects of hyperparathyroidism; review of sixty-three cases. *Surg., Gynec. & Obst.*, Aug., 1948, *87*, 172–182.

Sixty-three patients with proved hyperparathyroidism were observed at the Mayo Clinic through 1946. The disease was due to a single adenoma in 56 cases, to multiple adenomas in 3 cases and to diffuse primary hyperplasia in 4 cases. The ages of the patients ranged from the second to the seventh decade. Complications of the urinary tract were more common and more important than osseous complications.

About 20 per cent of the patients had generalized osteitis fibrosa cystica without renal complications. Somewhat less than 20 per cent had both renal complications and osteitis fibrosa cystica. Slightly more than 20 per cent had renal complications and some osteoporosis but not osteitis fibrosa cystica. Approximately 35

per cent had complications of the urinary tract and no evidence of osseous disease. Generalized osteitis fibrosa cystica was present in less than 40 per cent of cases while nephrocalcinosis or urinary lithiasis was found in more than 70 per cent.

The diagnosis was established with certainty in 3 cases in the absence of any complications on the basis of the characteristic changes in the content of calcium and phosphorus in the blood and urine. Since the disgnosis can be made with complete certainty, exploration of the parathyroid glands is never indicated to establish the diagnosis and the surgeon must accept the fact that in every case of hyperparathyroidism one adenoma or more or primary hyperplasia is present.

The treatment of hyperparathyroidism is surgical. Adenomas should be removed completely and in cases of diffuse primary hyperplasia, the hyperplastic tissue should be excised subtotally with the preservation of between 30 and 200 milligrams of hyperplastic tissue.—*Mary Frances Vastine, M.D.*

BREWER, LYMAN A., III, JONES, WILFRED, and DOLLEY, FRANK S. Non-malignant intrathoracic lesions simulating bronchogenic carcinoma. *J. Thoracic Surg.*, Aug., 1948, *17*, 439–463.

Thirty operated cases are presented in which although peripheral carcinoma of the lung was suspected, various benign lesions were found. This group consisted of 20 inflammatory conditions, 6 benign tumors, and 4 developmental abnormalities.

The diagnosis and differential diagnosis are discussed and diagrammatic representations of the roentgenograms are presented.

The difficulty of the clinical problem in the early diagnosis of bronchogenic carcinoma is emphasized by the fact that in only one-half of the cases treated by the authors could the carcinoma be diagnosed by bronchoscopy. Most often the differentiation between peripheral malignancies and non-malignant conditions cannot be made without exploratory thoracotomy. The authors believe that the management of a suspected case of peripheral bronchogenic carcinoma has reached a status similar to that of suspected carcinoma of the breast with exploration, biopsy, and radical excision, if cancer is proved.—*Frederick Reis, M. D.*

GROW, JOHN B., BRADFORD, MARTIN L., and MAHON, HUGH W. Exploratory thoracotomy in the management of intrathoracic disease. *J. Thoracic Surg.* Aug., 1948, *17*, 480–493.

Two hundred cases in which exploratory thoracotomy was performed for the diagnosis and treatment of obscure intrathoracic disease are presented. Malignant tumors occurred in 21.5 per cent of the cases. The accepted methods of differential diagnosis are discussed and their limitations indicated. The pathologic diagnosis of these cases and the roentgen appearance are shown in tables and several cases are illustrated by reproductions of roentgenograms.

A negative bronchoscopy is of no value in excluding intrathoracic neoplasm.

The accepted practice of using roentgen therapy as an adjunct in the diagnosis of malignant lymphomas is condemned because:

1. Not all malignant lymphomas respond to the roentgen therapy.
2. Many benign lymphadenopathies and resectable malignant lesions of the thymus do respond to irradiation and would lead to an erroneous diagnosis.
3. There are indications that the prognosis of localized mediastinal lymphoma is improved by combined resection and radiation therapy.
4. The prompt establishment of a histopathologic diagnosis expedites initiation of treatment.

About 25 per cent of circumscribed parenchymal lesions were found to be malignant. This emphasized the necessity of early exploration in undiagnosed lesions of this type.—*Frederick Reis, M.D.*

EVANS, BYRON H., and HAIGHT, CAMERON. Surgical removal of unsuspected mediastinal lymphoblastomas. *Arch. Surg.*, Sept., 1948, *57*, 307–324.

Four cases of mediastinal lymphoblastomas which simulated benign lesions are discussed. Two were Hodgkin's disease and 2 lymphosarcoma.

Single unilateral circumscribed mediastinal lymphoblastic tumors are uncommon. The roentgenologic picture closely simulates dermoid or teratomatous tumors. Even if suspected, their response to test doses of irradiation is so limited this method of differential diagnosis may be fallacious.

In 3 cases the correct diagnosis was not suspected. The fourth was not given a test dose of irradiation. Six previous cases removed surgically are discussed. One case of Hodgkin's disease in this series of 4 was given 400 r, in air, anteriorly and posteriorly one month after operation. The patient lived seven and one-half years. A case of lymphosarcoma was given 1,200 r, in air, anteriorly and posteriorly postoperatively and was well five years later. Two other cases, one of Hodgkin's disease and one of lymphosarcoma were well five years later, having no irradiation. A long survival without symptoms is not considered a cure because of possibility of late recurrences. It is not the authors' intention to remove isolated lymphoblastoma. It can be said that their patients were improved rather than harmed by operation.—*Thomas L. Martin, M.D.*

Westermark, Nils. Importance of intra-alveolar pressure in the diagnosis of pulmonary disease. *Radiology*, May, 1948, *50*, 610–618.

The degree of filling of the pulmonary vessels, of the capillaries and of the chambers of the heart is profoundly affected by the intra-alveolar pressure. Westermark demonstrates this by having the patient hold a tube from a water manometer in his mouth and varying the pressure from minus 15 cm. of water up to plus 80 cm. of water. Roentgenograms are taken at the proper pressures.

This method is of value in obtaining roentgenograms at various intervals in which the vascular structures remain at the same size, since standard conditions of intra-alveolar pressure can be maintained. He has also been able to demonstrate that the volume of the heart can increase by up to one-third when the pressure is low and decrease by one-third when a high pressure exists.

Roentgenograms made at normal levels and at high pressures will give a rough estimate of the pressure in the pulmonary arteries since the point at which the arteries in the hilum decrease in size can be determined.

Roentgenograms made during positive intra-alveolar pressure may reveal lymph nodes in the hilum not otherwise demonstrable, the diminished size of the vessels making the nodes more easily visible.

In moderate degrees of congestion, in pulmonary edema and in acute bronchopneumonia of an early stage, definite diminution or disappearance of some of the shadows can be demonstrated under high pressure conditions.

In acute lobar pneumonia, in atelectasis, in chronic pneumonia and in most cases of tuberculosis changes are minor or absent.

This is an interesting article and well worth reading in the original.—*Frank J. Rigos, M.D.*

Perry, S. Paul, and Shapiro, Robert. Suppurative bronchopneumonia with cavitation. *Radiology*, March, 1948, *50*, 351–364.

Seven cases of a rather bizarre type of bronchopneumonia characterized by parenchymal suppuration and necrosis with cavity formation have been added to the sparse radiologic literature pertaining to this entity. The patients were young adults and the incidence of this condition was 0.2 per cent of all cases of pneumonia observed at a naval hospital during a period of several months. All the reported cases recovered without complications under sulfonamide and penicillin therapy; hence, material for pathological study was not available. Cultures of sputum tended to implicate the B-hemolytic streptococcus as the etiological agent in 4 cases. Some of the cases followed in the wake of an epidemic of scarlet fever, and frequently there was a history of antecedent upper respiratory tract infection. The chief symptoms were fever, cough and the expectoration of purulent sputum; pleuritic pain was common. Physical and laboratory findings were not characteristic and the diagnosis depended primarily upon the roentgen demonstration of cavitation within an area of consolidation. Serial films combined with appropriate clinical and laboratory examinations were of particular value in differentiating the more severe forms from other diseases, such as tuberculosis.—*William N. Thomas, M.D.*

Kershner, Richard D., and Adams, W. E. Chronic nonspecific suppurative pneumonitis. *J. Thoracic Surg.*, Aug., 1948, *17*, 495–513.

Ten cases of chronic nontuberculous inflammation of the lungs are reported which present a clinical entity unlike that of lung abscess and bronchiectasis. It must be differentiated from bronchogenic carcinoma, chronic lung abscess, tuberculosis and bronchiectasis. The principal features of differential diagnosis are a gradual onset of synptoms without obvious cause, and

diffuse infiltration of the lungs without bronchial dilatation or cavity formation on roentgen examination.—*Frederick Reis, M.D.*

MACHLE, WILLARD, and GREGORIUS, FREDERICK. Cancer of the respiratory system in the United States chromate-producing industry. *Pub. Health Rep.*, Aug. 27, 1948, *63*, 1114–1127.

A high incidence of cancer of the lung had been noted by the management of a plant producing chromates. This stimulated a further study by the health committee of the chromate industry. Six plants were selected concerned with the extraction of chromate from ore.

The study was made by a statistical compilation obtained from mortality data of these plants and comparing them to other industrial plants for the control group.

The findings were a consistent high rate of deaths from cancer of the lung in the plants concerned. The individual ratios varied from 13 to 31 times the normal. The overall ratio was 16 times the expected ratio of 1.3 per cent. The increase was in both the groups of below the age of fifty years and the group above.

The deaths from cancer elsewhere were the same as in the control group. The ratio for penumonia was also higher in this group than in the control.

Evidence suggests that the carcinogenic compounds of chromium are the monochromates as this high rate of carcinoma of the lung was not found in the groups not exposed to this compound.

Roentgenograms of chests were not taken.—*Joseph Levitin, M.D.*

FARBER, S. M., BENIOFF, M. A., and TOBIAS, G. Primary carcinoma of the lung; diagnosis by cytological studies of sputum and bronchial secretions. *California Med.*, Aug., 1948, *69*, 95–99.

In bronchogenic carcinoma, tumor cells often exfoliate into the adjacent bronchial lumen. Demonstration of neoplastic cells in the sputum is a valuable early method of suggesting or establishing the presence of malignancy.

With careful collection, selection, preservation, and staining of sputum or bronchoscopic aspiration samples, using a technique similar to the Papanicolaou method of vaginal smear examination, a high diagnostic accuracy may be attained. Previous observers have demonstrated tumor cells in 84 to 89 per cent of patients with proved bronchogenic carcinoma. In the present authors' series of 52 patients with proved malignancy, 43, or 82 per cent, had positive or suspicious smears. In a series of 1,512 specimens from 414 patients suspected of having bronchogenic carcinoma, positive or suspicious cells were found in 69 patients, 56 of whom were subsequently shown to have bronchogenic carcinoma.

This technique is useful in the study of peripheral lesions not accessible to bronchoscopic biopsy, and in demonstrating malignancy in patients with pre-existing pulmonary tuberculosis. Failure to find tumor cells on a single specimen does not rule out the possibility of malignancy. In many of the author's patients, five or more specimens were examined before tumor cells were seen.—*Henry P. Brean, M.D.*

MOYSÉS, JOSÉ. Blastomicose pulmonar. (Pulmonary blastomycosis.) Brasil méd. cir., Sept., 1948, *10*, 497–500.

Blastomycosis has been described in the medical literature under different synonyms of which "Brazilian paracoccidiosis," "blastomycoid granuloma," "parablastomycosis," "Lutz' mycosis" or "Brazilian blastomycosis" are most frequently encountered in Brazil.

In autopsy studies pulmonary localization of the disease was observed in 84 per cent of the cases. According to Amadeu Filho the pulmonary manifestations of blastomycosis may be classified as (1) small lesions of granular type; (2) nodular well circumscribed acinous or acinodular lesions of predominantly granulomatous type; (3) extensive infiltrative lesions of predominantly granulomatous or exudative type; (4) abscesses; (5) ulcerative, more or less acute lesions, without evidence of encapsulation; (6) ulcerative, more chronic lesion, with evidence of encapsulation, and (7) nodular lesions with spontaneous regression.

The difficulty of the differential diagnosis from pulmonary tuberculosis is evident; in about 15 per cent of the cases, blastomycosis is associated with tuberculosis.

The clinical history (with roentgenograms) of a sixty year male patient, suffering from extensive bilateral exudative blastomycosis of the lungs and apparently completely cured by means of sulfadiazol, is presented in detail.—*Ernst Schmidt, M.D.*

Pendergrass, Eugene P., and Robert, Agrippa G. Some considerations of the roentgen diagnosis of silicosis and conditions that may simulate it. *Radiology*, June, 1948, *50*, 725–745.

Pneumoconiosis is a broad generic term used to describe all forms of pulmonary reaction to dust lodging within the lungs, with no implication as to character, severity, or effect on function. Certain of these reactions may be demonstrated by roentgen examinations of the chest, but in most instances they are entirely nonspecific, are unaccompanied by formation of progressive fibrosis, and are of no clinical significance. The authors recognize two clinically important specific pneumoconioses, namely silicosis and asbestosis, as well as a number of benign pneumoconioses resulting from the inhalation of a variety of inert but radiopaque dusts. The former may be productive of disability, whereas the latter are of clinical significance only because they may lead to errors in diagnosis through their ability to produce upon the roentgenogram a nodular pattern, at times indistinguishable from that occurring in silicosis.

For accurate diagnosis of silicosis there is necessary a positive history of sufficient exposure to free silica dust plus the roentgenologic demonstration of characteristic deviations from the normal within the lungs. Physical and laboratory examinations are then required to exclude other conditions producing similar roentgenographic changes.

Reproductions of roentgenograms are shown, again reiterating the various stages of the disease and also the importance of associated infections, both nonspecific and tuberculous. The histopathology of silicosis is reviewed in detail. Criteria of asbestosis diagnosis is not reviwed.

A considerable part of the treatise is concerned with the differential diagnosis of other inhaled dusts as well as other pulmonary manifestations of disease not produced by dust inhalations.—*E. A. Addington, M.D.*

Hatch, Theodore F. Significance of occupational history in diagnosis of silicosis. *Radiology*, June, 1948, *50*, 746–750.

Since the pulmonary changes of silicosis as revealed by the roentgenogram are not characteristic of that disease alone, an occupational history is an essential aid in accurate interpretation of the roentgenogram of the chest. There must be confirming evidence of sufficient exposure to silicosis producing dust before a diagnosis of silicosis can be made on the roentgenograms.

The thesis of this paper is a plea for more detailed study of particle size, composition in relation to particle size, and dust concentration in intermediate industries and occupations in which silicosis occurs sporadically. There is a definite danger in shortcut methods of assessing dust hazards, and the author points out why the usual methods are not accurate in these types of industries and occupations.—*E. A. Addington, M.D.*

Corcoran, William J. Anthraco-silicosis. *Radiology*, June, 1948, *50*, 751–754.

This is a review of observations made in coal miners with anthracosilicosis in the anthracite coal fields over a period of twenty-seven years.

It is the opinion of the author that when a man is exposed to a silica hazard, it takes from five to seven years before there were any distinctive changes in the lungs that can be noted on the roentgenogram. The diagnosis of anthracosilicosis cannot be made with any degree of assurance on the roentgenogram alone in the first stage. The history must be obtained. This is not true concerning the second and third stages of the disease. Their roentgenographic appearances are characteristic and the diagnosis can be made with less consideration of the history.

Fluoroscopy is a most valuable aid and has been much neglected in the evaluation of silicosis of the lungs. Also of value is the taking of films in inspiration and expiration.

Infection is not often encountered in either lung in the first two stages of the disease. It is in the third stage that infection occurs most frequently. After the age of fifty, and usually in the third stage, tuberculosis is more common in silicotic individuals than in those not so affected.

The author states that anthracosilicosis is a progressive incurable disease and then states he has never known of a case in which a first stage silicotic, after having been removed from the dust hazard, went on into a third stage silicotic. Those in the late second stage will go on into the third stage but will progress more slowly if they are removed from the hazard. The author has never seen an instance of total and permanent disability from anthracosilicosis

alone unless the disease had advanced well into the third stage.

A short discussion of protection methods is included. Investigation of the use of aluminum in counteracting the deleterious effects of silica is mentioned.—*E. A. Addington, M.D.*

PRINZEMETAL, MYRON; CORDAY, ELIOT; BERGMAN, H. C.; SCHWARTZ, LOIS, and SPRITZLER, R. J. Radiocardiography: a new method for studying the blood flow through the chambers of the heart in human beings. *Science*, Sept. 24, 1948, *108*, 340–341.

Passage of radioactive substances through the cardiac chambers can now be graphically recorded with a specially constructed, ink writing Geiger-Müller counter.

Technique is described, charts are included in the article and curves explained.

Two hundred and fifty subjects were given injections for study with no untoward effects. The amount of radiation is much less than the amount patient receives during various diagnostic roentgen examinations.

Studies on hemorrhagic shock, tetralogy of Fallot and determination of circulation time are mentioned.—*Anthony F. Rossitto, M.D.*

## ABDOMEN

EVANS, WILLIAM A. Obstructions of the alimentary tract in infancy. *Radiology*, July, 1948, *51*, 23–35.

This paper reviews the alimentary obstructions which occur in infancy and emphasizes their roentgen diagnosis. The basis of the paper is 400 cases of obstructing or potentially obstructing lesions.

Infantile hypertrophic pyloric stenosis reveals a persistently long narrow pyloric canal which can be seen fluoroscopically and spot filmed. It may be necessary to aspirate and lavage the stomach before giving the small (5–10 cc.) barium meal. Barium enema indicates the extension of intussusception into the colon and the degree of gaseous distention of the small bowel. Intussusception may be partially or totally reduced by the procedure. Esophageal atresia should be suspected in the newborn from the appearance of abundant frothy sputum in the mouth. Food and barium should be withheld. An opaque catheter passed into the esophagus will indicate obstruction. In atresia of the duodenum the stomach and duodenum proximal to the atresia are outlined by gas. Absence of gas in the lower small bowel and colon indicates complete obstruction. Roentgenologically, meconium ileus, volvulus and atresia of the ileum may be indistinguishable. A barium enema determines whether the gaseous distention is confined to the small bowel and also locates the cecum for evidence of a malrotation pointing to a volvulus. With imperforate anus the extent to which the bowel is patent can usually be determined in the inverted vertical position. Neither this method nor the lateral projection with the knees tightly flexed on the abdomen is without error.

Gas may not displace impacted meconium in the rectum. Meconium ileus can be recognized if there is no abrupt termination of the gas distended bowel and if there is emulsified gas and meconium. A barium enema examination will show a small lumen of the large bowel and an obstruction to the barium flow possibly in the region of the splenic flexure. The author states malrotation of the colon is the basis of volvulus of the mid-gut. Early in this condition there is evidence of obstruction of the duodenum; later, the jejunum and ileum become distended. Two cases are shown which gave clinical and roentgenographic evidence of obstruction where no anatomical obstruction existed.—*Oliver P. Winslow, Jr., M.D.*

SWENSON, PAUL C., and MANGES, WILLIS F. Roentgen findings in functional disturbances of the gastro-intestinal tract. *Radiology*, March, 1948, *50*, 365–377.

The normal and pathological physiology of the alimentary canal is discussed.

The esophagus exhibits three forms of muscular activity:

1. Primary pharyngeal contraction waves.
2. Secondary waves attributed to local mechanical stimulation. These act as true peristaltic waves and travel in both directions.
3. Tertiary contractions which give the esophagus a serrated appearance sometimes called "curling." These are increased in esophagitis and rarely marked in the normal organ.

If inflammation, neoplasm and obstruction can be ruled out the radiologist can conclude that dysphagia has its origin in the central nervous system or in some primary myopathy. Antral spasm and pylorospasm should be considered as due to local disease only when a

definite organic lesion can be shown. Ulcers should not be diagnosed on functional irregularities alone. Apparent pylorospasm will frequently disappear when food is mentioned to the patient.

Occasionally true antiperistalsis is seen in the duodenum. A partial regurgitation, not due to antiperistalsis, is frequently seen in the region of the superior mesenteric artery. This is considered a relatively normal physiologic obstruction. An organic obstruction may occur in anorexia nervosa due to weight loss and consequent dragging of the mesenteric root and its vessels over the distal portion of the duodenum.

Reflex motor disturbances from the stomach, diseases of the mesentery and retroperitoneal lesions, emotional states, allergic conditions and deficient nutrition can cause function disturbances of the small intestine.

Voluntary change of bowel habits, congenital anomalies and the use of cathartics can upset the functioning of the large bowel. Scybala in the rectum indicate disturbed motility. The rectum should be empty except during defecation.

The alimentary canal has its own inherent mechanism which can be modified and controlled by the autonomic nervous system. This secondary control may take a prominent part in the regulation of the entire tract or any portion thereof in functional diseases.—*Oliver P. Winslow, Jr., M.D.*

Ravitch, Mark M. Polypoid adenomatosis of the entire gastro-intestinal tract. *Ann. Surg.*, Aug., 1948, *128*, 283–298.

The author reports 2 interesting and unusual cases in which all segments of the gastrointestinal tract were involved in polypoid adenomatosis. At the autopsy of the first case, an eighteen month old white male, the mucosa from the cardia of the stomach to the anus was covered with innumerable polyps without "skip areas." A barium enema revealed the multiple polyps in the colon, but a small bowel study with the introduction of barium through a Miller-Abbott tube did not demonstrate polyps. The child died after operation for intussusception in the ileum.

In the second case, a sixteen year old white girl, an emergency exploratory operation revealed polyps of the stomach and several segments of the small bowel. Strangely enough these could not be demonstrated with repeated roentgenographic studies. She had peculiar brown pigment in irregular flecks on the lips and oral mucosa which was first described by Hutchinson in association with intestinal polyps.

Polypoid adenomatosis of the colon is a definite clinical entity with a familial incidence. In the review of the literature the author quotes the high incidence of malignant change in these cases and stresses the importance of complete colectomy. Adenomatosis of the small intestine often first manifests itself by intussusception. In the author's experience, polyps of the small intestine are difficult to demonstrate roentgenographically. All polyps of the stomach should be considered potentially malignant and subtotal gastric resection is advised as the treatment of choice.—*T. D. Allison, M.D., and C. L. Hinkel, M.D.*

Rigler, Leo G. Roentgen examination of the stomach in symptomless persons. *J.A.M.A.*, Aug. 21, 1948, *137*, 1501–1507.

The vast majority of persons coming to surgical treatment for carcinoma of the stomach are in the advanced stage of the disease and results are still exceedingly poor. Some means must be devised to discover carcinoma of the stomach when the lesion is small and in an early stage of development. Because of the insidious onset, diagnosis must be made before the development of any appreciable symptoms or physical signs. The only method which appears to be universally applicable and reasonably accurate is routine roentgen examination of the stomach. However, because the incidence of carcinoma of the stomach is relatively low, probably not more than three per thousand of the living population over the age of forty-five, the productivity of routine roentgen examination is of such an order as to discourage efforts to undertake it.

The first question which must be answered is whether or not the roentgen method is actually an accurate procedure for the diagnosis of early carcinoma of the stomach. The author has already had some experience in this field in previous studies on routine roentgen examination of the stomach in patients with pernicious anemia and achlorhydria. He has demonstrated that it is possible to diagnose extremely small polypi and also small carcinomas. Nevertheless, it must be admitted that when small lesions are being searched for the percentage of error

will rise appreciably and positive errors will likewise be increased in their frequency.

In the practical consideration of the feasibility of extensive routine examinations of symptomless persons certain short cuts should be considered. One of these is the selection of groups of persons in whom the incidence of carcinoma would be greater than in the general population. Certain factors which seem to be associated with or to precede carcinoma of the stomach (age; family history of carcinoma of the stomach, pernicious anemia or achlorhydria; atrophic gastric mucosa; gastric ulcer; occult blood in the stool) are not sufficiently definitive to be of practical use in selection of cases. Achlorhydria and hypochlorhydria are common accompaniments of gastric cancer. By gastric analysis of all persons past the age of fifty, followed by roentgen examination for all those who show achlorhydria or hypochlorhydria, the vast majority of carcinomas should be discovered. Pernicious anemia is another condition closely associated with carcinoma of the stomach as established by previous studies. Repeated examination at semiannual intervals of patients with pernicious anemia results in the detection of a considerable number of early cancers of the stomach; however, only 5 per cent of persons with carcinoma of the stomach have pernicious anemia.

Another short-cut would be the development of means by which the roentgen examination might be rendered less arduous, time consuming and expensive. Use of fluoroscopy alone would eliminate the expense of the film examination, but would not eliminate the time required of the radiologist. It is generally conceded that small lesions may be overlooked even by experienced fluoroscopists. Examination by films alone eliminates the expense of the time spent by the radiologist in fluoroscopy, but if the examination is to be accurate, the large number of films involved and the elaborate technique necessary to make an adequate examination would result in considerable expense. The conventional method of a combination of fluoroscopy, spot-filming, and roentgenographic examination is undoubtedly the most accurate but is expensive and time consuming. Photofluorography materially reduces the expense of the examination and the time consumed by the radiologist. None of these short-cuts is entirely satisfactory and the comparative accuracy of the various methods in diagnosing small lesions needs to be evaluated. It seems reasonable to propose that a number of studies be undertaken on a small scale by these various methods in order to ascertain how accurate each is and how rapidly and inexpensively they could be achieved.

The author reports his results in a study of a series of patients selected with three criteria in mind. All patients were over the age of fifty, had no particular gastric symptoms and showed either achlorhydria or free hydrochloric acid of less than 30 units. Roentgen examination of the stomach was done at semiannual intervals. Five hundred forty-four such persons were examined. Fourteen cases of gastric carcinoma were discovered and one additional should have been found, but was missed as a result of error in interpretation. Eleven of the cases did have remote or minor symptoms and therefore did not fall into the category of truly symptomless persons. In addition, there were 9 patients with gastric polypi and numerous other abnormalities such as hiatus hernia, duodenal deformity and enlarged gastric rugae. The author concludes that the studies indicate the feasibility and value of routine roentgen examination of symptomless persons in selected groups for the discovery of gastric tumors.—*Leslie K. Sycamore, M.D.*

WARREN, RICHARD, and LANMAN, THOMAS H. Surgery in bleeding peptic ulcer. *Surg., Gynec. & Obst.*, Sept., 1948, *87*, 291–298.

*Summary and Conclusions*

1. The use of methods of nonsurgical treatment of massive bleeding from peptic ulcer has always resulted in a small percentage of cases which come to the surgeon because medical measures have failed. In these cases, especially if there has been a prolonged trial of such a medical regimen, the postoperative mortality is high.

2. Early "urgent" operation is, therefore, advocated on all patients with massive hemorrhage from peptic ulcer who are over 45 years of age and in whom the hemorrhage persists after 48 hours following admission to the hospital (or having stopped, recommences).

3. Subtotal gastrectomy with removal of the lower two-thirds of the stomach, including the pylorus, should be the surgical plan for these patients.

4. In those patients in whom the ulcer is

technically difficult to remove, a subtotal gastrectomy with exclusion, but not removal, of the ulcer is advocated. In patients with a large inflammatory mass involving the pylorus and duodenum, a two stage subtotal gastrectomy as described by McKittrick should be done.—*Mary Frances Vastine, M.D.*

Partington, Philip F., and Sachs, Maurice D. Routine use of operative cholangiography. *Surg., Gynec. & Obst.*, Sept., 1948, *87*, 299–307.

The need for additional diagnostic methods to improve the results in gallbladder surgery has long been acknowledged. The possibility that careful study of diagnostic methods other than operative ones might improve results led Mirizzi, Best, Hicken and others to the use of immediate or operative cholangiography.

The purpose of this paper is to report the authors' results with the routine use of operative cholangiography on all patients requiring gallbladder or common duct surgery during the year 1946–1947.

*Technique.* The only special equipment necessary is a plywood tunnel which is placed beneath the patient's lower thorax and abdomen without an intervening mattress. This tunnel is large enough to hold a 14 by 17 inch cassette and a grid. The surgeon places a tie on the cystic duct close to the gallbladder to prevent injection of radiopaque material into the gallbladder. The authors use 70 per cent diodrast as the contrast medium. It is injected through a small needle after being warmed to body temperature. The needle is inserted into the common duct and 20 cc. of the material is injected slowly. The exposure is made during a period of respiratory arrest induced by carbon dioxide. Intratracheal nitrous oxide, oxygen and ether constitute the anesthetics used.—*Mary Frances Vastine, M.D.*

Bullock, W. K., and Edmondson. H. A. Pancreatic lithiasis and calcification. *California Med.*, Aug., 1948, *69*, 104–108.

Pancreatic lithiasis may be asymptomatic, or associated with intermittent upper abdominal pain, elevated serum lipase and amylase levels, and hyperglycemia. Later, diabetes mellitus and steatorrhea may appear. The appearance of calculi following one to fourteen years of chronic pancreatitis has been described. Many but not all patients are alcoholics.

Pancreatic calcification may be demonstrated on plain films of the abdomen. In the lateral view, calculi in the head and body of the pancreas lie just anterior to the lumbar spine; calculi in the tail lie more posteriorly, in the plane of the lumbar vertebral bodies. Calcification may be in the form of separate intraductal stones, or in a very fine stippled calcification usually involving all or most of the gland. Duodenal aspiration after intravenous injection of secretin may show lack of the normal increase in bicarbonate and pancreatic enzymes. The stools may show undigested fat, and the glucose tolerance test may reflect damage to the islets of Langerhans.

Twenty-two cases of pancreatic calculi and calcification were found by the authors in a series of 35,000 necropsies, an incidence of 0.062 per cent, comparable to the incidence of 0.044 per cent previously reported in another large postmortem series. However, careful dissection of a series of postmortem pancreases after postmortem roentgenography by Lüdin uncovered 28 cases in 542 pancreases, an incidence of 5.1 per cent.

Clinical features in the authors' 22 cases, in order of frequency, were weight loss, jaundice, enlarged liver, upper abdominal pain, weakness, nausea, vomiting, constipation, edema, ascites and steatorrhea. Seven patients had diabetes mellitus, and 10 were alcoholics. Eleven had cirrhosis of the liver at autopsy.—*Henry P. Brean, M.D.*

Hiatt, Robert B., and Wilson, Paul E. Celiac syndrome. VII. Therapy of meconium ileus; report of eight cases with a review of the literature. *Surg., Gynec. & Obst.*, Sept., 1948, *87*. 317–327.

The association of meconium ileus with pancreatic cystic fibrosis was first described by Landsteiner in 1905. Since then there have been 11 other cases reported in each of which meconium ileus has been noted at operation and fibrocystic disease of the pancreas described following autopsy. Thus the coexistence of these two conditions has been well established. Seven additional cases have been found in the pathological records of the Babies Hospital.

Two hypotheses have been suggested to explain the association of abnormal meconium and fibrocystic disease of the pancreas. The first, advanced by Landsteiner, regards the abnormal meconium as primary and the

changes in the pancreas as the result of intestinal obstruction; the second considers the changes in the pancreas as primary and the abnormality of the meconium as the consequence of lack of normal digestion of the meconium by pancreatic secretions. The latter view, which is generally held at present, has been strongly supported by the studies of Farber.

*Summary*

1. Eight cases of meconium ileus are described. All of the infants presented signs of intestinal obstruction soon after birth and came to operation as soon as their disturbance of water and electrolyte balance had been corrected.

2. A new technique is described for the removal of obstructing meconium by irrigation through an ileostomy wound and milking out of bulky masses so as to re-establish the intestinal channel. Postoperative drainage is not required.

3. In 5 cases there was an associated volvulus of a loop of ileum, presumed to result from excessive writhing of elongated and hypertrophied coils of small gut proximal to the obstructing inspissated meconium. In 4 of these cases the volvulus was corrected by simple unwinding; in 1 case resection of gangrenous bowel was required; and in 2 cases failure to recognize the gravity of the circulatory impairment at the time of operation was a contributory cause of the unfavorable outcome.

4. In all 8 cases the existence of associated cystic fibrosis of the pancreas was established. The authors believe that pancreatic insufficiency underlies all instances of meconium ileus. The history of pancreatic fibrosis or of meconium ileus in a sibling supports the preoperative diagnosis of meconium ileus in a newborn infant with intestinal obstruction.

5. Five of the 8 patients coming to operation were successfully relieved of intestinal obstruction. The oldest of the survivors is now more than two years old. The prognosis of the survivors is dominated by the underlying pancreatic disease.—*Mary Frances Vastine, M.D.*

## GENITOURINARY SYSTEM

ZATZKIN, HERBERT R. Effective compression in excretory pyelography. *Radiology*, May, 1948, *50*, 639–644.

The author describes a method of technique in intravenous pyelography whereby he places the cuff of a baumanometer beneath the customary compression band that is attached to most roentgenographic tables. The lower edge of the cuff is about 2.5 cm. above the symphysis with the tubes leading from the cuff directed inferiorly.

It is stated that the renal sinuses are better visualized, thus approaching the density of retrograde pyelography and that the resulting dilatation of the ureters and pelvis of the kidney is not objectionable.—*C. H. Warfield, M.D.*

BRODNY, M. LEOPOLD, and ROBINS, SAMUEL A. Urethrocystography in the male child. *J.A.M.A.*, Aug. 21, 1948, *137*, 1511–1517.

Urethrocystography is a simple, painless and safe substitute for endoscopic examination which is applicable in many urinary problems in infants and children. A study of 250 male patients under sixteen years of age is reported by the authors.

The examination is indicated in suspected obstructive uropathy, persistent or recurrent pyuria, nocturnal and diurnal enuresis and other symptoms related to the lower part of the urinary tract, in the evaluation of postoperative results and in the study of physiology of micturation. Contraindications are urethral bleeding, acute local infections and recent instrumentation.

Two methods of study are employed: voiding and retrograde, the former depicting the physiologic state of micturation; the latter visualizing the anatomy of the urethra in a state of distention. The medium used is "rayopake" in 20 per cent dilution for cystography and 50 per cent for urethrography. For cystography the bladder is filled to tolerance and anteroposterior and oblique views are taken. In urethrography an oblique film is taken while the patient voids into a nonopqaue plastic container. An anteroposterior view is also taken during a second voiding. Urethrograms can be obtained similarly after excretory urography, and the authors recommend this as a routine procedure in children.

The retrograde method is performed by means of a special penile clamp with syringe, the exposure being made while the injection is in progress.

The anatomy and roentgenographic anatomy of the male urethra are described in the article.

The major pathologic conditions for which

the procedure is of value are classified in five groups: congenital anomalies, obstructive uropathies, infections, neuromuscular dysfunction and control of surgical status. Hypospadias, congenital stricture of the urethra, congenital valves, congenital fistulae and diverticulum and reduplication of the urethra are examples of congenital conditions amenable to diagnosis by this method. Of the obstructive uropathies, hypertrophy of the internal sphincter and inflammatory or traumatic strictures of the urethra and stricture of the external meatus are among the conditions observed commonly. In the group of infections, chronic cystitis may sometimes be diagnosed roentgenographically in the presence of negative urinary findings. Acute cystitis, urethritis and prostatitis have characteristic roentgen findings. In neuromuscular dysfunction the cystourethrogram is useful in localizing the involved muscular components. Finally, the procedure is useful in recording the anatomic and functional status following surgical treatment of the lower part of the urinary tract and in following the course of recovery.—*Leslie K. Sycamore, M.D.*

Fisher, R. S., and Howard, H. H. Unusual ureterograms in a case of periarteritis nodosa. *J. Urol.*, Sept., 1948, *60*, 398–404.

Periarteritis nodosa involves the urinary tract in over 80 per cent of cases. The authors report a case occurring in a thirteen year old girl who was admitted to the hospital with a painful rigid abdomen, which relaxed a few hours after admission. Migratory joint pains developed two days later and persisted for several weeks. A maculopapular rash appeared on the extremities four days after admission. Chills and fever developed later. An intravenous urogram showed excellent concentration of dye in both kidneys. This dye was still present at sixty minutes. The upper thirds of both ureters were markedly dilated and spastic.

The symptoms recurred intermittently over a period of several weeks. An exploratory laparotomy showed an enlarged liver with spider-web like streakings in the capsule. Gradual abdominal distention, oliguria and elevation of the non-protein nitrogen occurred and were followed by generalized convulsions and death. Pathological examination showed an inflammatory and proliferative process involving the smaller arteries and arterioles of the kidneys, ureters and gallbladder. This vascular reaction was most marked in the adventitial connective tissue of the ureters. The regional lymph nodes of the ureters were markedly hyperplastic. The anatomical diagnosis was periarteritis nodosa.

The authors feel that the ureterographic picture of moderate dilatation with marked spasticity is not found in other conditions and may be a specific finding in periarteritis nodosa.—*Rolfe M. Harvey, M.D.*

Cottler, Z. R. Nonhormonal adrenal cortical carcinoma. *J. Urol.*, Sept., 1948, *60*, 363–370.

Most of the emphasis has been placed on hormone-producing tumors of the adrenal cortex. The scarcity of reports on the nonhormone-producing tumors is due to their rarity, the absence of early symptomatology, and the confusion as to the primary site of a tumor when metastases are present due to the fact that carcinomas of other organs frequently metastasize to the adrenals.

Nonhormonal adrenal tumors are discovered late through the presence of a mass, vague abdominal pains, malaise, poor appetite and evidence of metastasis. The average duration of symptoms is one year and the tumors occur in adults over thirty.

Diagnostic aids include 17-ketosteroid urinary excretion studies, electrolyte and vitamin C balance studies, perirenal air insufflation, excretory urography and laminagraphy.

The treatment of the nonhormonal type of tumor has been surgical removal followed by high voltage therapy. The prognosis is poor.

The author reports the case of a fifty year old female who was admitted to the gynecological ward of the hospital for a "fallen womb." Abdominal palpation disclosed a large hard mass in the right flank, separate from the liver. The blood pressure was 290/170. Excretory urography showed depression and deformity of the pelvis and calyces of the right kidney. A barium enema showed extrinsic pressure effect on the right colon. A lateral pyelogram showed marked anterior displacement of the right kidney. A preoperative diagnosis of right renal neoplasm was made. At operation a tumor mass was found attached to the right kidney. Microscopic examination of the tumor was reported as adenocarcinoma of the adrenal. Following operation the blood pressure dropped to 136/76. Roentgen therapy, 2,500 r, was given postoper-

atively to each of our fields centered over the site of the lesion.

A recurrent mass was noted in the right mid-abdomen thirty months later and an additional 4,000 r was given to two fields. The mass was unchanged four months later and the same course of therapy was repeated. A recurrence in the left abdomen was noted five months later and deep roentgen therapy was given to this side of the abdomen. Mediastinal metastases were first noted thirty-nine months after operation. These were also treated by deep roentgen therapy, 1,500 r to an anterior and posterior field.

The remarkable points in this case are the maintenance of a normal blood pressure for five years following removal of the tumor, and the five year survival period with extensive abdominal and mediastinal recurrences which were present for at least twenty-seven months.—*Rolfe M. Harvey, M.D.*

KRETSCHMER, HERMAN L., and MCDONALD, J.K. Carcinoma of the bladder with bone metastases; report of 8 cases. *Surg., Gynec. & Obst.*, Sept., 1948, *87*, 328–337.

The old idea that bone metastases secondary to carcinoma of the bladder are of rare occurrence seems still to prevail. In a previous communication one of the authors reported 5 cases and called attention to the fact that this condition occurs more frequently than is appreciated and that it may occur with small papillary tumors that appear to be simple papillomas.

*Summary*

1. Bone metastases in carcinoma of the bladder occur more frequently than is generally appreciated.

2. Papillary carcinoma was the type of tumor in each case in the authors' series.

3. In 1 case bone metastases were present although there was no evidence of bladder tumor at the time of entering the hospital.

4. In this series the type of bone lesion was osteolytic.

5. Bone metastases in bladder carcinoma occur reasonably early in the course of the disease.

6. It may be the cause of the first symptoms that bring the patient to the doctor.

7. Routine roentgen-ray examination in all cases of papillary tumors of the bladder may reveal the presence of bone metastases when least suspected.—*Mary Frances Vastine, M.D.*

ROBINS, SAMUEL A., and FISCHMANN, JOSEPH. Hydronephrosis; radiologic classification based on anatomical variations. *Radiology*, May, 1948, *50*, 632–638.

Anatomically hydronephrosis is classified as internal, combined or external according to its relationship to the kidney parenchyma. Internal hydronephrosis designates dilatation restricted to the intrarenal portion of the kidney and external hydronephrosis designates dilatation of the renal pelvis. The combined type involves both the calyces and the pelvis and is the most common type.

The width of the kidney parenchyma seen on the roentgenograms is a reliable index of the extent of damage resulting from the hydronephrosis.

The authors believe that the type of hydronephrosis and the measurement of the width of the renal parenchyma should be included in the roentgenographic report because this helps to describe the pathological anatomical process occurring within the kidney.—*Frank J. Rigos, M.D.*

SKELETAL SYSTEM

PONSETI, IGNACIO. Evolution and treatment of tuberculosis of the hip. *Surg., Gynec. & Obst.*, Sept., 1948, *87*, 257–276.

The evolution and the results of conservative and operative treatments were studied in 31 proved cases of tuberculosis of the hip followed for a minimum period of four years. This work was done in the Department of Orthopedic Surgery in the State University of Iowa Hospitals.

1. The first group of patients, all children, had a para-articular focus of tuberculous osteitis. In the granulous osteitis the roentgenograms show a small area of uniform bone destruction whereas one or several small bone sequestra are seen in the area of destruction due to caseous osteitis. Both types have a tendency to heal under prolonged conservative treatment. However, the hip joint in each of the 7 patients was invaded sooner or later by the tuberculous process.

The hip joint was slowly destroyed when lesions of tuberculous granulation tissue with no

caseation predominated while the hips were destroyed rapidly when lesions of caseation necrosis were present. Once the hip joint became involved it either fused spontaneously or a fusion operation had to be performed because of persistent pain and deformity.

It is proposed that the treatment of tuberculous osteitis close to the hip joint be directed toward obtaining an ankylosed joint as soon as the local process is quiescent and the general condition of the patient is favorable.

2. The second group consisted of 15 patients with tuberculous arthritis of the hip joint with onset during childhood. In 8 of the patients the arthritis was probably synovial in origin. Treatment must aim at fusion. The optimum time for surgery is during the third year of the disease when the patient's general condition is good and the roentgenograms show a sound reossification of the atrophic bone.

3. The third group comprised 9 patients of adult age with hip tuberculosis. Its evolution varied widely and in many cases the hip condition closely paralleled the pulmonary status.—*Mary Frances Vastine, M.D.*

Esguerra-Gomez, Gonzalo, and Acosta, Emilio. Bone and joint lesions in leprosy; radiologic study. *Radiology*, May, 1948, *50*, 619–631.

Four hundred and eighty-three lepers had roentgenographic examinations of their hands and feet. Three hundred and six of these patients had clinical evidence of involvement of the hands and feet and all of these had roentgenographic changes. In the remaining 167 patients without clinical signs of skeletal involvement, 68 per cent revealed decalcification, rarefaction, atrophy, hypertrophy or hyperostoses. This indicates the importance of a routine roentgenographic study of the hands and feet of all individuals having a diagnosis of leprosy. The article contains good illustrations of all the roentgenographic phases of the disease.—*Frank J. Rigos, M.D.*

Bromer, Ralph S., and Harvey, Rolfe M. The roentgen diagnosis of rickets associated with other skeletal diseases of infants and children. *Radiology*, July, 1948, *51*, 1–10.

The roentgen diagnosis of rachitic skeletal involvement associated with infantile scurvy, congenital syphilis and lead poisoning are discussed and illustrated. The authors found no cases of rickets associated with erythroblastic anemia or sickle cell anemia. They cite such a case reported by Caffey in 1937. Reference is also made to a previously reported case of rickets occurring in a case of osteogenesis imperfecta.

In combined cases the signs of scurvy tend to obscure those of rickets. Rickets combined with congenital syphilis results in a masking of the latter, in the experience of the authors. Until rickets starts to heal there will be no "lead line" in lead poisoning combined with rickets. Rickets and scurvy can develop and be recognized in osteogenesis imperfecta.—*Oliver P. Winslow, Jr., M.D.*

Neuhauser, Edward B. D., Schwachman, Harry, Wittenborg, Martin, and Cohen, Jonathan. Progressive diaphyseal dysplasia. *Radiology*, July, 1948, *51*, 11–22.

Four cases of a rare syndrome are presented and illustrated. The clinical findings consist mainly of retardation of growth in height, weight, and muscular weakness.

Pathologically, there is a thickening of the periosteum beneath which is an altered cortex with evidence of progressive active bone resorption and deposition which alters the cortex to a cancellous type bone. No cartilaginous elements are seen. The marrow is altered to a loose fibrous tissue with collections of mononuclear and hematopoietic cells in small numbers. All of the changes are considered nonspecific and no suggestion is given as to the etiology.

Roentgenologically, one finds bilaterally symmetrical fusiform enlargement of the diaphyses with an amorphous thickening of the cortex. The dense cortex is sharply demarcated with loss of normal trabeculation. Lesions progress proximally and distally along the long axis of the bone. The extremities are long for the size of the child and the muscles are underdeveloped. No changes were noted in the epiphyses or metaphyses.

The authors suggest progressive diaphyseal dysplasia as a descriptive term for this syndrome.—*Oliver P. Winslow, Jr., M.D.*

Coley, Bradley L., Higinbotham, Norman L., and Bowden, Lemuel. Endothelioma of bone. *Ann. Surg.*, Sept., 1948, *128*, 533–560.

In this paper a series of 91 histopathologically proved cases of Ewing's sarcoma is carefully analyzed. Of this group, 73 cases are five

year follow-ups with a resultant survival rate of only 4.1 per cent. This is regardless of the treatment used which included: surgery, irradiation and surgery, irradiation alone, and Coley's toxins. In discussing the distinguishing characteristics of this disease entity, the authors point out that Ewing's sarcoma is a disease of youth seen in males in a ratio of 2:1 with the majority of the primary sites below the waistline, often accompanied by fever and leukocytosis, and frequently diagnosed as osteomyelitis in its early phases. The origin of the tumor is stated to be in the medullary or subcortical portion of the bone, but this remains open to question as is brought out in the discussion. Pain, swelling and disability, the usual triad of symptoms with malignant bone tumors, are present in most cases. Metastases are early and widespread, involving bones, notably the skull, as well as the lungs. The authors stress that biopsies should be taken in all suspected cases before treatment as small doses of roentgen therapy may distort and mislead the histopathologic interpretation. The roentgen appearance of extensive involvement of the shaft with irregular cortical destruction and subperiosteal new formation with the "onion skin" appearance may be typical, but more often than not the appearance is atypical. The roentgen differential diagnosis includes osteolytic osteogenic sarcoma, reticulum cell sarcoma of bone, metastatic neuroblastoma, osteomyelitis, and occasionally eosinophilic granuloma. In this series pathological fractures are seen in 21 per cent of the cases and neurological disorder occurs in 16 per cent. The authors emphasize the extremely poor prognosis of this disease. As various methods of treatment have yielded uniformly poor results, the authors recommend palliation by roentgen therapy. The bibliography is well selected and comprehensive.—*T. D. Allison, M.D., and C. L. Hinkel, M.D.*

SHERMAN, ROBERT S., and STERNBERGH, WALDEMAR C. A. The roentgen appearance of ossifying fibroma of bone. *Radiology*, May, 1948, *50*, 595-609.

Twelve cases of ossifying fibroma of bone are reported by the authors. Six involved the maxilla, 5 the mandible and 1 the temporal bone. Pathologically ossifying fibroma of the jaw is not specific. The clinical and roentgenographic features are believed to be more characteristic than the pathological.

Clinically the disease occurs typically in childhood, being discovered as a painless swelling of the face which slowly enlarges over a period of months or years. In later life the growth rate slows down. Ocasionally symptoms were present due to the growth effect of the tumor such as nasal obstruction, proptosis, tearing of the eye and deafness.

The best method of treatment is curettage of the tumor area. Resection of the tumor was done in a few of the larger tumors. Irradiation appeared to have little or no effect.

The roentgenographic findings are those of a unilocular lesion usually limited to the maxilla or mandible, oval to spherical in shape with a distinct boundary usually of an egg shell character. In the mandible the tumor arises within the medulla; in the maxilla the tumor may arise from the medulla or subperiosteally. In its early phase the process is predominantly osteolytic with little or no internal architecture and no periosteal reaction. Enlargement is progressive, with an increased productive element brought about in the maxilla by the formation of spherical densities and in the mandible by irregular striae. In the maxilla the adjacent bone may be dissolved without pressure displacement.

Several excellent illustrations are included.—*Frank J. Rigos, M.D.*

CAMP, JOHN D., and SCANLAN, ROBERT L. Chronic idiopathic hypertrophic osteo-arthropathy. *Radiology*, May, 1948, *50*, 581–594.

Chronic idiopathic hypertrophic osteo-arthropathy, not associated with primary disease, is rather a rare condition. The authors report 5 cases and review 20 other cases reported in the literature. This disease occurs predominantly in males at the age of puberty or adolescence and is characterized by the osteo-arthropathic syndrome—clubbing of the digits, enlargement of bones and joints and thickening of the skin of the face in the absence of any demonstrable primary disease.

Clinically the disease is slow and insidious in onset, with a slowly progressive course, which after many years gradually comes to a halt. Symptoms are few. Fatigue, excessive sweating and vasolability are common. Secondary sexual disturbances such as hypertrophy of the breast, feminine distribution of hair and scanty growth of the beard are also common. The joints may be involved with a real arthritis, a sterile effusion, pain, limitation of motion and systemic

reactions. The skin changes are due to increased fibrous tissue in the dermis and subcutaneous tissues. Large folds of skin are seen sometimes resembling gyri of the brain.

The striking roentgenologic feature is an accentuation of lateral growth in the bones symmetrically distributed and best seen in the long bones. Bone proliferates subperiosteally. The medullary cavity is not constricted. The proliferation is greatest over the diaphyses decreasing in extent to the epiphyses. The distal phalanges are usually not involved and the ungual tufts undergo absorption or atrophy. The bones are of normal length with normal epiphyses and joints. Secondary osteo-arthropathy is the only disease which can cause an identical appearance. The acute onset, rapid progression and the association with the primary disease differentiates the secondary type from the chronic idiopathic variety.

The authors speculate about a possible relationship to the pituitary gland or to the hypothalamus. Treatment is symptomatic.—*Frank J. Rigos, M.D.*

Fairbank, H. A. Thomas. Melorheostosis. *J. Bone & Joint Surg.*, Aug., 1948, *30-B*, 533–543.

This article is taken from an Atlas of General Affections of the Skeleton and is the third in number. Subjects previously published were on osteogenesis imperfecta and osteopetrosis. Melorheostosis is a very rare condition in which certain bones or parts of bones are petrosed. It displays striking differences from generalized osteopetrosis or "marble bones." Fairbank briefly describes the distinguishing features as: (1) the changes, in typical cases, are confined to the bones of one limb; (2) the outline of an affected bone is, sooner or later, distorted; (3) there is often pain, occasionally severe, sometimes unbearable; (4) there is limitation of movement in the joints formed by the affected bones. None of these features is invariably present.

In the paper, the literature is briefly reviewed, followed by the etiology, age and sex incidence and the distribution of the petrosis. In more detail the symptoms and signs, the complications, roentgenographic appearance, progress, pathology and diagnosis are discussed. Brief case reports are given with the reproductions of the roentgenograms of the bone lesions.

Fairbank regards the diagnosis in a typical case as easy. In generalized osteopetrosis every bone is affected to some extent, and the distribution of the density in the individual bones differs markedly from that seen in melorheostosis. From osteopoikilosis the differentiation is also easy, provided that the whole roentgenographic evidence is considered and that undue attention is not paid to the appearance of one or two epiphyses. Other conditions to be differentiated are multiple diffuse fibrosis of bone (polyostotic fibrous dysplasia) and Albright's syndrome. No difficulty should be experienced in distinguishing the condition from inflammatory sclerosis.—*R. S. Bromer, M.D.*

Fairbank, H. A. Thomas. Osteopoikilosis. *J. Bone & Joint Surg.*, Aug., 1948, *30-B*, 544–546.

This paper is the fourth installment taken from an Atlas of General Affections of the Skeleton. Osteopoikilosis or osteopathia condensans disseminata is an unusual affection of the skeleton characterized by multiple dense spots in many bones. The age and sex incidence, roentgenographic appearance and distribution, the progress of the condition, complications, pathology and diagnosis are discussed. Roentgenograms of two cases are reproduced.

The dense spots, as described in the paragraph on the roentgenographic appearance, are circular, ovoid, or lanceolate, the long axis being parallel to the long axis of the affected bone. They vary in size between 2 and 10 millimeters. They occur in the epiphyses and adjacent parts of the metaphyses and are plentiful in the short bones of the carpus and tarsus. In most cases they are numerous and are found in every bone with the exception of the skull, ribs and vertebrae. Even in these bones, one or two spots have been seen, the skull being the most unusual site of all. The spots are in the cancellous bone and as a rule they are entirely free from the cortex which is never distorted in any way. Sometimes a spot of dense bone is prolonged into a short streak, in the axis of the bone, especially when it is situated some distance from an epiphyseal line where the metaphysis of a major long bone is passing into the shaft. In the shaft itself spots are seldom seen. Cases have been observed over a number of years with no apparent change in the roentgenographic appearances.—*R. S. Bromer, M.D.*

BLOOD AND LYMPH SYSTEM

BLEICH, ALAN R., and KIPEN, CHARLES S. Venous calcification in Banti's syndrome. *Radiology*, May, 1948, *40*, 657–660.

A case history is presented in which the diagnosis of Banti's disease was made and the spleen removed seventeen years before the present admission.

On the present admission the roentgenogram showed a density running transversely across the upper mid-abdomen and lying behind and below the stomach in the region of the pancreas. Surgical exploration proved the density to be calcified splenic vein and portal vein. The case is presented for rarity in demonstrating calicified abdominal veins other than phleboliths.—*C. H. Warfield, M.D.*

WESTERMARK, NILS. Studies of the circulation by roentgencinematography. *Radiology*, June, 1948, *50*, 791–802.

The author reviews some of the concepts of cardiovascular physiology and circulation time with particular reference to the fact that the ventricles do not empty by displacement of the apex and lateral contours of the ventricles toward the center of the heart but through displacement of the atrioventricular junction downward toward the apex. He reports from his previous investigations on the hearts of sheep that a metallic indicator placed at the atrioventricular junction made a sudden downward movement toward the apex. This movement began during or immediately after the QRS complex. About half way between the S and T the indicator made a rapid return to the original position which was reached at the beginning of T. From these experiments it appears that both the downward phase and the returning phase of the piston-like movement of the atrioventricular junction takes place during systole, while this junction remains relatively quiet during diastole.

The present report is based on studies of the circulation as recorded by cinematography of the fluorescent image produced by exposure to roentgen rays. An electrocardiogram has been taken simultaneously with the roentgen cinematography. A description of the equipment is given. The films show the contrast material (thorotrast) as it flowed through the heart (rabbit) and the rapid piston-like displacement of the atrioventricular junction toward the apex and its equally rapid reverse movement is reported to have been demonstrated. The pulmonary circulation time as seen on the films varied between 1.2 and 2.5 seconds with a mean value of 1.5 seconds. Previous investigations showed the mean time of the entire circulation at approximately 18 seconds.

In interpreting the course of the systolic contraction it seems probable that the systolic contraction of the ventricle begins with a contraction of the interventricular septum, in which the septum is shortened and the central part of the atrioventricular junction drawn toward the cardiac apex. In connection with the contraction of the septum and the movement of the atrioventricular junction toward the apex, the papillary muscles emanating from the septum will contract and prevent the atrioventricular valves from being forced into the auricles. The contraction will then proceed continuously along the septum to the cardiac apex. —*Robert K. Arbuckle, M.D.*

ROENTGEN AND RADIUM THERAPY

PENDERGRASS, EUGENE P., and MAHONEY, J. FRANCIS. A consideration of roentgen therapy in producing temporary depilation for tinea capitis. *Radiology*, April, 1948, *50*, 468–475.

Tinea capitis has been epidemic in the Eastern United States since 1943. The principal fungus is *Microsporum audouini*. The epidemiology, the usual clinical course of the disease and method of diagnosis are described.

Temporary epilation of the scalp by roentgen ray is the treatment of choice having demonstrated a very favorable percentage of cures.

In enumerating the advantages and disadvantages of roentgen treatment, the authors emphasize the safety of the procedure. It is a painless treatment performed at one sitting with a high cure rate. The patient becomes practically non-infectious at the end of three weeks. The possibility of permanent depilation is small and believed due to the disease rather than the effects of roentgen therapy.

Procedure—local treatment is discontinued for at least one week before roentgen depilation is undertaken. Hair is clipped short. A closed-portal technique individualized to varied head head shapes is described. Technical factors are 75 kv. (peak), 18 ma., no added filter and a focal skin distance of 26 cm. Each field is

given 500 r (in air). This method of treatment has given a higher rate of cure than the previously employed Adamson-Kienböck technique.—*E. E. Seedorf, M.D.*

Donlan, Charlotte P. Tumor dose in cancer of the larynx. *Radiology*, April, 1948, *50*, 463–467.

The author presents a classification for 113 cases of cancer of larynx treated at Presbyterian Hospital, New York. Reviews classification, technique and results of various authors showing that the tumor dose customary today is approximately 5,000 r. With some change in technique following 1928 to 1936 period, there has been little increase in the survival rate. Lesions restricted in the vocal cord gave the highest survival rate.—*E. E. Seedorf, M.D.*

Nohrman, Bengt A. Quelques espériences tirées de traitements du cancer du sein par rayons x associés à l'opération d'Halsted. (Some experiences drawn from treatment of cancer of the breast by roentgen irradiation combined with Halsted operation.) *J. de radiol. et d'électrol.*, No. 7–8, 1948, *29*, 403–407.

This paper is from the Radiumhemmet, Stockholm, Service of Prof. E. Berven, and contains many wise precautions and statements essential to the correct discussion of the entire problem of therapy of breast cancer. Nohrman reports 769 cases of cancer of the breast treated at Radiumhemmet from 1936–1941. The cases were treated by irradiation combined with Halsted operation (radical mastectomy and dissection of axillary nodes). All patients were observed at least five years and the tumor tissue subjected to rigid microscopic study. The author shows that a clinical classification of Steinthal's type is not adequate; the best classification is based on the histopathological examination of the axillary nodes. The cases of this compilation have been classified according to these principles. The importance of different factors is discussed: degree of extension of axillary metastasis, age and death from intercurrent disease, menopause, selection of cases, roentgen treatment before and/or after operation. He concludes that preoperative roentgen treatment makes the prognosis better in the group which comprises the cases with the worst prognosis (15 per cent of all cases). As it is impossible to decide with certainty before the operation to which group or which stage the cases belong, every patient suffering from cancer of the breast should be given preoperative irradiation. Lastly, the value of postoperative irradiation can be considered as firmly established.—*William M. Loehr, M.D.*

Maisin, J. Le rôle des radiations dans le traitement du cancer du sein. (The rôle of irradiation in the treatment of cancer of the breast.) *J. de radiol. et d'électrol.*, No. 7–8, 1948, *29*, 363–400.

The purpose of this report is to evaluate treatment of cancer of the breast by irradiation as an adjunct to surgery and treatment of breast cancer by irradiation alone. The author is Director of the Cancer Institute at the University of Louvain and this article was the second report presented before the VI Congress of French-Speaking Radiologists held at Geneva, July 27–31, 1948.

In his Avant-propos the author shows the necessity of revising classical notions on the treatment of carcinoma of the breast.

He then gives a detailed analysis of surgical statistics. This is necessary from the fact that Halsted's surgical treatment has been the classical treatment of carcinoma of the breast for the last fifty years. According to this investigation cancers of Stage I Steinthal have good surgical results; 65 per cent cases of survival after five years can be considered the figure. For Stage II cases surgical results after five years are mediocre, 25 per cent is an average number. It must be noted that Stage II carcinoma is much more frequent than Stage I. The average survival of Stage I and Stage II cases is 35 per cent.

It seems logical, then, to look for better results in a surgical-irradiation combination or in irradiation alone.

Postoperative radiotherapy has been more frequently employed than preoperative, or the two combined. Postoperative radiotherapy distinctly improves surgical results, particularly in cases of Steinthal's Stage II, in which survival after five years is almost doubled.

In Stage I cases, results are improved, but this is difficult to prove owing to the high percentage of survivals due to surgery only. For both Stage I and Stage II the average survival after five years is 50 per cent.

The Edinburgh school strongly recommends mastectomy followed by postoperative irradia-

tion (50 per cent after five years, Stage I and II).

The combination of roentgen irradiation with wide radium puncture without other surgical interference than a biopsy gives almost equal results as postoperative radiotherapy (51 per cent after five years). Steinthal's Stage IV cases give only palliative results. Survivals after five years are rare.

The value of hormone therapy and castration as contributing factors to other treatments is discussed.—*William M. Loehr, M.D.*

THAYSSEN, VIGGO E. The influence of castration by roentgen on carcinoma of the breast. *Acta radiol.*, 1948, *29*, 189–204.

The author presents material from the Radium Center in Copenhagen which consisted of 99 breast cancer cases with metastases or recurrences. All of these cases were treated with roentgen irradiation of the ovaries and in one-third improvement resulted. A comparison with 100 control cases which were not subjected to castration therapy shows that 40 per cent of the castrated were still living two years after the appearance of the metastases as against only 11 per cent of the controls. Of 74 pre- or postoperatively roentgen treated and castrated, 28 per cent were alive five years after the operation as against 8 per cent of the controls. On the basis of 79 urine assays for gonadotropin and estrogen it is shown, among other things, that the castration may have a highly beneficial effect even in cases where the estrogen output was low before castration.—*Mary Frances Vastine, M.D.*

LEWIS, LLOYD G. Radical orchiectomy for tumors of the testis. *J.A.M.A.*, July 3, 1948, *137*, 828–832.

The author bases his treatment of testicular tumors on their radiosensitivity as determined by Friedman,* and in line with this he offers a clinical -pathologic classification. After simple orchiectomy, the tumor can be accurately classified and the proper selection of treatment made. This is either irradiation, extended surgical treatment or combined therapy.

The seminoma comprises 44 per cent of the 250 cases, and is characterized by relatively slow growth, late but inoperable metastases and marked radiosensitivity. About 1,000 roentgens are necessary for prophylactic or definitive therapy. Treatment is thus logically taken care of by simple orchiectomy followed by postoperative irradiation with 1,000 roentgens delivered to the nodes.

The tumors of definite embryonic cells, undifferentiated or adenocarcinoma, comprise 11.27 per cent of the series, and are characterized by rapid growth, early metastases and sensitivity to irradiation somewhat less than the seminoma since a dose of 2,000 or 3,000 roentgens is necessary to destroy this group. Orchiectomy followed by 250,000 volt roentgen therapy is inadequate and radical resection of the retroperitoneal nodes is done.

The presence of chorionic tissue distinguishes two related groups of tumors. The trophocarcinoma developing from the cytotrophoblast comprises 6.8 per cent and the chorionepithelioma from syncytotrophoblast comprises 4.8 per cent. These are the hemorrhagic tumors which metastasize by way of the blood stream as well as the lymphatic system and are radioresistant, requiring 5,000 to 6,000 roentgens for destruction. Prophylactic irradiation is therefore contraindicated and radiation therapy confined to inoperable metastatic involvement.

The remaining tumors are made up of various types of teratocarcinomas; the exact type depending on whether the malignant cells take the form of seminomas, embryonal carcinomas, choriocarcinomas, chorionepitheliomas or the form characterized by malignant change in the undifferentiated tissue itself. In all these tumors, however, there are either adult or embryonic structures derived from more than one primitive germ layer. They are cystic and may be recognized on gross examination. They are very radioresistant.

A description of the operative procedure of resection of the retroperitoneal nodes is given. This procedure is advocated either with, or in the cases of the very resistant tumors, without associated roentgen treatment for all malignant tumors of the testicle except the seminoma. There was no operative mortality in 169 cases. —*F. H. Squire, M.D.*

MUSGROVE, JAMES E., and MCDONALD, JOHN R. Extra-abdominal desmoid tumors. *Arch. Path.*, April, 1948, *45*, 513–540.

The authors define desmoid tumors as usually solitary benign fibrous neoplasms originating from musculo-aponeurotic structures and having the peculiar characteristic of locally invad-

* Friedman, M. *S. Clin. North America*, 1944, *24*, 1424.

ing striated muscle. They occur most frequently on the abdominal wall.

This paper is a clinico-pathological study of 34 cases of extra-abdominal desmoid tumors removed surgically at the Mayo Clinic in the thirty-eight years through 1945. The tumor occurs in a wide age distribution predominantly (70 per cent) in females. The authors discuss the traumatic and endocrine theories of etiology and elaborate extensively on the pathological features.

Radical excision is the treatment of choice. Recurrence follows incomplete removal. The tumor is almost completely radioresistant. The authors feel that if irradiation is used at all it should be used in cancerocidal doses. Castration or other endocrine therapy may be helpful in inoperable cases.—*D. D. Beiler, M.D., and C. L. Hinkel, M.D.*

Schmitz, Herbert E., and Towne, Janet E. The treatment of pelvic endometriosis. *Am. J. Obst. & Gynec.*, April, 1948, *55*, 583–590.

One hundred thirty patients with pelvic endometriosis have been studied and divided into four groups according to the method of treatment. These groups are: (1) surgical group, (2) irradiation group, (3) hormone group, and (4) untreated group. Some of these patients are included in more than one group. They have been followed from one to four years.

Since pelvic endometriosis occurs most frequently in the child-bearing period and is a major cause of sterility, conservative treatment which will increase the possibility of conception is desirable. Forty-three and nine tenths per cent of the 130 cases treated were treated by surgical procedure. Ten, or 17.6 per cent, required radical surgery. Forty-seven, or 82.4 per cent, had one or both ovaries preserved, and 11 later conceived, giving birth to 13 infants. Roentgen therapy was used in 29 cases, of which 17 were given sufficient dosage to cause permanent menolysis. Twelve were treated with smaller dosage causing a menolysis of from three to eight months. In this group 2 conceived and delivered 3 infants, an incidence of conception of 16.6 per cent. Roentgen therapy in this group proved satisfactory for secondary therapy when conservative surgery had failed. Roentgen therapy of sufficient intensity to destroy ovarian function is indicated in cases where endometrial tissue has invaded bowel or bladder. It obviates the necessity of surgical resection with its increased risk.

Watchful expectancy or male hormone therapy is of value in cases with minimal disease and symptoms in young women. It enables one to postpone more radical procedures to the years when such therapy is less costly.—*Wendell C. Hall, M.D.*

Brunschwig, Alexander. Complete excision of pelvis viscera for advanced carcinoma. *Cancer*, July, 1948, *1*, 177–183.

Brunschwig describes a radical operative procedure for total excision of all pelvic viscera which has been carried out on 22 patients with advanced carcinoma. Most of these had received irradiation previously without control of the growths. Many had pain, fistulas, and ureteral involvement. No selection of cases was made except that the disease must be confined to the pelvis.

After thorough preoperative preparation, the bladder, lower ureters, pelvic colon, uterus and adnexa, including contents of obturator fossae, are mobilized through a low midline excision. A sigmoid colostomy is done and both ureters are transplanted into the sigmoid. A perineal approach is then made to remove these viscera with complete resection of the vagina and anus. The resultant "wet colostomy" is handled by a Rutzen bag cemented to the skin.

The primary operative mortality was 23 per cent. It is not claimed that this operation is more than a palliative procedure although several patients are living without evidence of disease four to eight months later. They returned to normal physical activity. This is attained despite the fact that all patients were in terminal stages of disease prior to operation, and presented the usual criteria of inoperability.—*J. A. Campbell, M.D.*

Miller, Norman S. Carcinoma of the uterus, ovary and tube. *J.A.M.A.*, Jan. 17, 1948, *136*, 163–169.

Discussion of the management of cancer of the female generative organs is based on experience with 100 per cent follow-up of almost 2,500 patients during the past fifteen years at the University of Michigan Gynecological Tumor Conference.

Sixty-five per cent of all cancers of the female generative organs arise in the uterine cervix.

The advanced state of these cancers when first seen is assessed chiefly to (*a*) the underdeveloped program of periodic health examinations and (*b*) delay on the part of patients in seeking medical advice after the onset of symptoms. The chance of cure decreases approximately 16 to 20 per cent per month after the onset of symptoms (spotting). Cervical cancer is 90 per cent epidermoid, and 10 per cent adenocarcinoma which spreads chiefly by direct continuity or through the lymphatics, occasionally obstructing the rectosigmoid or metastasizing to bone. Death frequently results from ureteral stenosis, and less commonly from pulmonary metastases and infection. The principal and commonly only symptom of cervical cancer is irregular spotting or bleeding. Diagnosis should be proved by biopsy in every case.

Miller states that clinical grouping is the most important single factor in determining prognosis. The two acceptable treatments for cervical cancer are (1) irradiation by high voltage roentgen rays and radium, and (2) radical hysterectomy of the Wertheim type with bilateral salpingo-oophorectomy and pelvic lymphadenectomy. The latter is confined only to selected cases and there is not yet sufficient evidence that such surgery has more to offer than properly applied radiation.

Endometrial adenocarcinoma of the uterine corpus constitutes 15 per cent of all genital tract cancers. Clinical grouping is less satisfactory than in the cervix and is based on size of uterus, parametrial extension, and degree of uterine fixation. Postmenopausal spotting is the commonest symptom with 25 per cent showing only semipurulent leukorrhea, and 5 per cent no symptoms. Diagnosis may be suspected or proved by cytologic smears. The definite proof of malignancy and origin of such cells should come from uterine curettage, more dependably done in a hospital under anesthesia. Advanced cases permit no choice of treatment than high voltage roentgen radiation plus multiple capsule intrauterine application of radium which may result in cure. This method is also used in early cases whose health precludes major surgery. In all other cases, external irradiation or intrauterine radium is followed in six to eight weeks by total hysterectomy and bilateral salpingo-oophorectomy to remove any remaining active neoplastic cell nests.

Ovarian carcinoma amounts to 10 to 20 per cent of the total, affects chiefly postmenopausal women, and escapes early detection except by periodic pelvic examination. The degree of malignancy varies from the fast growing teratomatous to the slow growing papillary cyst adenocarcinomatous types. Diagnosis rests on cytologic study of ascitic fluid or histopathologic analysis of a surgical specimen. Solid ovarian masses or cystic enlargements of more than 5 cm. size, especially if showing progressive growth, call for surgical removal. Hysterosalpingo-oophorectomy is recommended for proved cases. Preoperative or postoperative roentgen therapy is desirable in all but extremely early lesions in young women in whom a normal ovary is left. Such therapy may make the lesion operable or occasionally may prolong life a decade or more.

Fallopian tube neoplasms account for only 0.1 per cent of genital cancers and are of the papillary adenocarcinoma type. Secondary carcinoma of the tube may occur from primary ovarian or uterine cancer. Diagnosis is made from cytologic smear, biopsy through the culde-sac or laparotomy following the discovery of a firm or nodular movable mass in the tubal area. Treatment consists of surgical extirpation of both tubes, ovaries, and uterus in operable cases. Roentgen therapy is given postoperatively and in inoperable cases.—*J. A. Campbell, M.D.*

DIDDLE, A. W., and BENNETT, T. R. Carcinoma of the cervix in an urban population. *Am. J. Obst. & Gynec.*, April, 1948, *55*, 669–675.

This article deals with experience in treating cervical carcinoma in Dallas, Texas between Jan. 1, 1936 and Jan. 1, 1946. Data for this study were obtained from metropolitan hospitals, private radiologic clinics, and the Registrar of Vital Statistics of the City of Dallas. Some of the records were very incomplete. Valuable information was also obtained from four of the pathology laboratories in the city. Data were obtained for 1,134 women with carcinoma of the cervix, probably representing at least 90 per cent of the new patients seen with cervical cancer in the city during the ten year period. Succeeding discussion is based on 992 women for whom the histopathologic diagnosis was available.

One-third of the women in the group were referred from smaller communities in Texas, Arkansas, Louisiana, and Oklahoma while the

other two-thirds lived in the city. An equal number of women were in the pre- and postmenopausal period. Eighty per cent were white and the remainder Negro or Mexican. Five per cent of the women were under thirty years of age. The youngest patient was nineteen and the oldest was eighty-seven years of age.

Most of the women sought consultation for vaginal bleeding or leukorrhea. It is impossible to correlate the duration of symptoms with the clinical grade of the tumor. The average delay from the onset to the time a diagnosis was made was 7.14 months; 6.4 wasted by the patient and 1 by the physician.

Sixty of the patients had adenocarcinoma and 932 epidermoid carcinoma. Fifty-seven were Stage I (Schmitz classification), 171 were Stage II, 302 were Stage III, 174 were Stage IV, and 290 were unclassified. Five hundred and thirty patients were treated with roentgen rays and radium. Eighty-nine had total hysterectomy and irradiation. (Sixty of the total hysterectomies were performed after cancer was suspected and the other 29 were done without suspecting cancer.) Subtotal hysterectomy and irradiation were used on 99 cases. Other gynecologic procedures and irradiation were used in 10 cases. Treatment information was incomplete in 264 cases. The use of both roentgen rays and radium gave better results than either alone or in combination with total hysterectomy. The prognosis for those women who developed cancer in the cervical stump after subtotal hysterectomy was almost as good as for those who had cervical carcinoma with the fundus present. The survival rate was decidedly diminished for those who originally had a subtotal hysterectomy for unsuspected cancer probably because of two factors: more time was wasted in giving proper treatment and the growth of the tumor was aggravated. Radiation treatment gave as satisfactory results for adenocarcinoma of the cervix as for epidermoid carcinoma. Nearly one-fourth of the women traced had known sequelae, exclusive of pain, attributed to the malignancy or to the treatment. Sequelae were about 50 per cent more common among patients having pelvic operations than among those who were unoperated. This relationship was particularly true where extrapelvic metastases and local recurrence with vaginal hemorrhage developed. Vaginal fistulas were three times more common among women who were irradiated repeatedly than among those given only one course of treatment.—*Wendell C. Hall, M.D.*

Marks, Joseph H., and Wittenborg, Martin H. Results of treatment of carcinoma of the ovary with data on the age incidence of this disease. *Surg., Gynec. & Obst.*, Nov., 1948, *87*, 541–545.

A review of the literature on malignant epithelial tumors of the ovary leaves some doubt as to the value of roentgen therapy in this disease. Most of the previously reported series of cases show little if any benefit as a result of such therapy. Most authors have recommended that roentgen treatments be given as a palliative measure in the more advanced cases. They have admitted that the dosage given to many of the patients was less than optimum as judged by present standards.

The authors report a series of patients seen in the department of roentgenology of the New England Deaconess Hospital during the ten year period beginning in June, 1936. The series consists of 76 patients, 57 of whom have now been followed to death. Of the original group, 14 were alive more than five years after their first operation and treatment, but 3 of the 14 have since died of their disease. One is alive at five and a half years with recurrent disease. Not all of the patients have as yet had an opportunity to live five years after treatment, but the five year survival rate calculated by the method of Nathanson and Welch is 21 per cent.

The original plan of treatment called for 1,800 roentgens (measured in air) to each of four pelvic ports. Treatments were given at 400 kilovolts with 50 centimeter target to skin distance and with a filter of 0.9 millimeter tin, 0.25 millimeter copper, and 1.0 millimeter aluminum. The usual daily dose was 300 roentgens to a single port and treatments were given daily except Sundays.

*Conclusions.*

1. Roentgen therapy should be employed in *all* cases of carcinoma of the ovary. This therapy is excellent insurance postoperatively even when the surgeon believes that all disease has been removed. Occasionally it may result in curve even in advanced stages of the disease.

2. The surgeon should not take too great risk in his attempt to remove the last fragments of diseased tissue. He should remove the easily accessible masses and then rely on roentgen

therapy in adequate dosage and through whatever ports may be necessary to cover the involved areas.

3. Roentgen therapy may bring about gratifying palliation even when cure is not obtained. It often gives relief of pain and causes a retardation of the production of peritoneal and pleural fluids.

4. The age specific incidence of cancer of the ovary is unlike that of most other types of malignant epithelial tumors since it falls after the sixth decade.—*Mary Frances Vastine, M.D.*

CAHAN, WILLIAM C., WOODARD, HELEN Q., HIGINBOTHAM, NORMAN L., STEWART, FRED W., and COLEY, BRADLEY L. Sarcoma arising in irradiated bone; report of eleven cases. *Cancer*, May, 1948, *1*, 3–29.

The authors have analyzed the literature, both laboratory and clinical, and come to the following conclusions: that the production of sarcoma in bone following irradiation is an uncommon sequel, which may take place whether normal or abnormal bone has been irradiated; whether malignant or benign lesions have been irradiated; that 3,000 roentgens are probably required to produce this change; that the malignant change requires from five to twenty-five years to take place. No explanation is given for the infrequent development of sarcoma in ribs, maxilla and jaw other than the possibility that these patients have malignant diseases from which they die before an observation of developing sarcoma is made.

It is believed by the authors that this complication of irradiation will become progressively less common as more radiologists restrict their activity to malignant diseases of bone. Particular attention is drawn to the inherent tendencies of giant cell tumors to undergo malignant changes, and it is the authors' opinion that roentgen radiation, an agent that in itself may provoke malignant changes, should not be used.—*W. E. Childs, M.D.*

CRAVER, LLOYD F. The nitrogen mustards; clinical use. *Radiology*, April, 1948, *50*, 486–493.

The history of discovery of usefulness of nitrogen mustards is given. Particularly subject to damage are the lymphoid tissues of the thymus, spleen, and lymph nodes, the bone marrow and the intestinal mucosa. Drug most widely used and employed by author is methyl-bis (beta-chloroethyl) amine hydrochloride. The method of use is described. With continued experience, dosage has increased now consisting of 0.2 mg. per kilogram body weight given intravenously on two or three successive days. Dosage is guided by total white blood cell count which decreases after administration.

Local toxic effects are occasional thrombosis and, if a leak into surrounding tissues, local inflammation. General toxic effects are mainly nausea and vomiting.

None of the nitrogen mustards have shown ability to cure any type of cancer. Palliative results have been seen in generalized Hodgkin's disease with marked constitutional symptoms, advanced cases of lymphosarcoma and anaplastic carcinomas of the lung.

In early and intermediate stages of Hodgkin's disease, in most cases of lymphosarcoma, and in most cases of chronic leukemia, it seems doubtful that nitrogen mustard offers any advantage over roentgen therapy.—*E. E. Seedorf, M.D.*

BURCHENAL, JOSEPH H. The newer nitrogen mustards in the treatment of leukemia. *Radiology*, April, 1948, *50*, 494–499.

Originally most widely used nitrogen mustard was methyl bis (2-chloroethyl) amine hydrochloride, known as HN2. Author reports experience with new nitrogen mustard derivative, 1:3 propane diamine NNN'N' tetrakis-(2-chloroethyl) dihydrochloride, known as SK 136. Administration is 0.1 mg. per kilogram of body weight daily for four to eight doses. New drug produced less nausea and vomiting among patients with chronic myelogenous leukemia, but patients with Hodgkin's disease had as much or more nausea as when HN2 was used.

Another derivative, SK 137, was discontinued because of increased toxic effect with no offsetting advantage. As with all other known forms of therapy, patients with chronic myelogenous leukemia progress from a state of sensitivity to treatment to one of resistance. Treatment of acute leukemia is unsatisfactory. SK 136 may be valuable in some patients which have become refractive to roentgen therapy and some in which the liver and spleen is of normal size. In general, roentgen therapy is more versatile and more effective.—*E. E. Seedorf, M.D.*

## RADIOISOTOPES

Wright, H. P., Osborn, S. B., and Edmonds, D. G. Rate of flow of venous blood in the legs measured with radioactive sodium. *Lancet*, Nov. 13, 1948, *2*, 767–769.

The author describes a direct method of measuring the rate of venous blood flow in the leg using a radioactive isotope $Na^{24}$ and a Geiger-Müller counter recording on a kymograph drum.

In 121 normal people the mean foot-groin flow time was $18 \pm 0.9$ sec. The range was 4–50 seconds.—*J. S. Summers, M.D.*

Rowlands, S., Rowley, D., and Stewart, H. D. Absorption and excretion studies with radioactive penicillin. *Lancet*, Sept. 25, 1948, *2*, 493–495.

Urinary excretion studies were carried out in female cats using penicillin labelled with $S^{35}$. Intramuscular injections gave rise to a urinary excretion of 100 per cent of the radioactive sulfur isotope, but there was a much smaller recovery of penicillin.

Oral administration gave much less excretion. The amount of radioactivity remaining in the gut at the end of the experiment suggested that non-absorption would account for that not present in the urine.—*J. S. Summers, M.D.*

Smith, Robert E., and Bronson, John F. An improved radioactivity measuring cup. *Science*, June 4, 1948, *107*, 603.

The authors describe the manufacture of a specimen cup used for the measurement of radioactivity in samples of either biological or chemical origin. A solution containing the active isotope is placed in a plain sample cup obtained commercially and which is stamped by a die of tool steel to give the desired concentric circular embossments.

Sample cups of the design reported here have been successfully used by the authors in measuring $P^{32}$, $I^{13}$ and $C_0^{60}$. $C^{14}$ or $S^{35}$ have not been studied.—*Anthony F. Rossitto, M. D.*

## MISCELLANEOUS

Epstein, Bernard S. Laminagraphy through plaster casts in postreduction roentgenography of congenitally dislocated hips. *J. Bone & Joint Surg.*, July, 1948, *30-A*, 778–780.

Epstein advocates the use of the laminagraph to secure better detail in roentgenograms of patients with congenital dislocation of the hips following reduction. Overexposed roentgenograms, taken with the use of the Potter-Bucky diaphragm, in his experience have been for the most part inadequate. The alignment of the hips cannot be adequately seen through the plaster casts.

The technique used is 150 milliampere-seconds, 55 to 60 kilovolts, target-film distance of 30 inches and Par Speed screens. The Kieffer laminagraph is employed using a five-turn spiral motion. Sometimes the five second exposure is too long for the patient to keep quiet, but, if the examination is performed while the child is anesthetized, this difficulty may be overcome. Otherwise, a two second exposure with two spiral turns is made, the kilovoltage or milliampere-seconds being raised to compensate for the diminished exposure.

He advises a preliminary roentgenogram based on an estimation of the height of the hips from the table top. Inspection of the wet film will determine whether or not the proper plane is in focus, and succeeding exposures can be made, as necessary. In his experience, the hips of infant patients were usually brought into sharp focus at 4.5 to 6 cm. from the table top. Occasionally, the femora will be so fixed that they are in slightly different planes. Separate exposures are then required, each thigh being placed so that the hip and femur lie parallel to the cassette. Attendants holding the patient should wear rubber gloves for protection.—*R.S. Bromer, M.D.*

Jacobson, L. O., Marks, E. K., Gaston, E. O., Simmons, E. L., and Block, M. H. Studies on radiosensitivity of cells. *Science*, March 5, 1948, *107*, 248–250.

Experiments performed tend to show that erythroblast vulnerability to irradiation injury is not enhanced by increased mitotic activity and proliferation. In fact, the hyperplastic erythroid tissue sustained less histologic injury than the normal. This is in contradistinction to the common belief that the more active the proliferation the more sensitivity to irradiation.

Whole body roentgen irradiation, 800 r, was applied to normal rabbits and those in which increased erythropoiesis was induced by phlebotomy or by the hemolytic action of acetyl phenylhydrazine on the circulating erythrocytes. In the former, the erythropoietic tissue

in bone tissue and spleen was essentially destroyed completely, but in the latter only partially destroyed.—*Anthony F. Rossitto, M.D.*

MURPHY, J. B., and STURM, E. The effect of growth or retrogression of a transplantable lymphosarcoma of the rat on the lymphoid organs and the adrenals of the hosts. *Cancer Research*, March, 1948, *8*, 139–142.

Investigation shows that the weight of the thymus, lymph nodes, and spleen in rats with actively growing transplanted lymphosarcoma is reduced. On the other hand, these organs increase in weight in rats with regressing transplanted lymphosarcomas. The adrenals of rats with progressing tumors were found to be about 25 per cent above normal weight while the adrenals in rats with regressing tumors was found to be about 30 per cent above normal weight. The reason for the above described changes cannot be clearly explained.—*John DeCarlo, Jr., M.D.*

SKAGGS, L. S., ALMY, G. M., KERST, D. W., and LANZL, L. H. Development of the betatron for electron therapy; with an introduction on the therapeutic principles of fast electrons. *Radiology*, Feb., 1948, *50*, 167–173.

Originally used for treatment of superficial skin lesions in 1928, the cathode ray, or electron stream, is again being investigated as higher voltage generators have increased the penetration possible. The betatron is the best method yet devised.

Unlike roentgen rays or gamma rays, the damage to normal tissue is not the limiting factor in their use on deep-seated lesions. The concentration of energy in a beam of fast electrons is at the end of the beam, not at the source. The beam range is limited by the voltage used in producing it. Therefore, one can concentrate the energy in the tumor, not in the surrounding or overlying tissues.

In this work a 22 million volt betatron at the University of Illinois was used.

The betatron accelerates electrons by injecting them into a circular vacuum chamber, called a donut, between the poles of an alternating current electromagnet. As they reach acceleration, the diameter of the electron orbit is expanded. A magnetic shunt is then used to deflect them out of the field and into the emerging stream. At a distance of 1 meter, an ionization equal to 100 r per minute of roentgen rays was produced. At 35 cm. an ionization of 1,500 r per minute with an 8 sq. cm. field was observed.

The beam measures 2.6 mm. as it emerges. Through air, the beam measures 6×13 at 10 cm., and 2×4 cm. at 35 cm. distance. Through a vacuum the beam remains smaller and much better defined.

A 13 mev. stream showed a penetration of 6 cm. through presdwood and it is calculated that a 35 mev. beam will penetrate 17 cm.

Ionization has not yet been measured, but it is expected to show slight increase from the surface to a point near the end of the range, with a sharp decrease to near zero, the exit dose being very small.

Collimation of the beam is simple, using wood and plastics.—*George D. Adams, M.D.*

SHULL, C. G., and WOLLAN, E. O. X-ray, electron, and neutron diffraction. *Science*, July 23, 1948, *108*, 69–75.

Neutron diffraction, the newly developed field in studying the atomic, molecular and crystalline structures, apparently has advantages in some problems over the older fields of roentgen-ray and electron diffraction.

Simple examples of such determinations have been carried out and charts and photographs are included in the paper. The most important applications were connected with the location of hydrogen or denterum positions.

From studies made there seems to be no serious obstacle in the way of extending the technique to more complicated cases, especially where denterated compounds can be used. It may become a useful tool in the study of the structures of organic compounds.

Since complicated structure determinations are very time consuming, rapid progress cannot be expected. Furthermore, the requirement of a chain-reacting pile as a source will make progress slower than by roentgen-ray and electron diffraction, for which adequate sources can be procured by any laboratory.—*Anthony F. Rossitto, M.D.*

CHARLES L. MARTIN

Janeway Lecturer, 1949